BIOLOGICAL ASPECTS OF THE TRANSMISSION OF DISEASE

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BIOLOGICAL ASPECTS OF THE TRANSMISSION OF DISEASE

EDITED BY

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FOREWORD

The Institute of Biology performed a valuable service in organizing a symposium of this nature. Not only was the subject of disease transmission one of considerable scientific interest and importance, but one which appealed to an audience recruited from many branches of biology

[illegible]

the unsolicited appreciation that was expressed by speakers and audience alike It was both refreshing and stimulating to attend an occasion on which botanists, zoologists, medical and veterinary

[illegible]

tribute to the work of the Institute's Conferences Committee and

[illegible]

C Horton-Smith

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THE DISPERSAL OF FUNGI PATHOGENIC FOR MAN AND ANIMALS

THE DISPERSAL OF FUNGI PATHOGENIC FOR MAN AND ANIMALS

By

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[illegible]

endemic in many widely separated geographical regions, are more sporadic while a third category is characterized by a high incidence in restricted geographical regions

Infections of the first type are characteristically endogenous [illegible]

mycoses in which there is pulmonary involvement. It seems reasonable to assume that these relatively unspecialized pathogens are spread from one individual to another by direct contact and by [illegible]

children caused by *Microsporum audouini* appears to have had its primary focus in western Europe where it still frequently occurs in [illegible]

specialized for the attack of certain races or are influenced by certain environmental factors and the possibility of a saprophytic phase must be borne in mind. For example, a case of *T. ferrugineum*

infection in man when introduced into western Europe does not initiate an epidemic outbreak (Vanbreuseghem, 1955), neither does *M. audouini* become epidemic, at least in the native population, when introduced into a tropical country. On the other hand, *M. audouini* has been introduced, presumably by emigrants from western Europe, into both temperate North America and Australasia where during recent years large scale epidemics have occurred in white school children. Whether the failure of *M. audouini* to establish itself on native children in the tropics and the failure of *T ferrugineum* to become established in temperate regions is due to environment[illegible]
is uncertain
Ceylon and
Europe and
" human " [illegible]

Similarly the infection of man or animals by " animal " dermatophytes such as the cattle ringworm fungus (*T. verrucosum*) can take place by contact or via farm gates or other structures which [illegible]

animals. During recent years *M gypseum* has been isolated on a number of occasions from the soil in different parts of the world [illegible]

stronger. *S schencki* has been shown experimentally to be pathogenic for certain plants (Benham and Kesten, 1932) and so the dispersal of this fungus potentially pathogenic for man is presumable from plant to plant Under conditions of temperature and humidity which favour the development of the fungus on plants or plant debris, and which can sometimes be broadly defined (Mackinnon, 1949), the fungus is introduced into man via a chance injury, frequently of the hand.

boydii. On the other hand the practice of going bare-foot is more usual in hot climates and thus the chances of infection are increased. As for sporotrichosis, there is no evidence of spread of infection between man and man. Dispersal occurs during the saprophytic phase and man, particularly male agricultural workers, accidentally

gillosis are probably the concentration of spores in the air and a lowered resistance of the host. The disease is frequent in captive wild birds and in young chickens kept under unhygienic conditions in brooders.

A striking example of a localized mycosis of high incidence is provided by coccidioidomycosis (*Coccidioides immitis*), which is

the significance of which may only be recognized by the positive skin reaction to coccidioidin (the extract of *C. immitis*) and the immunity conferred against progressive and fatal infection. The incidence of coccidioidomycosis is highest during the dry months of the year (with peaks following dust storms) and lowest during the wet season and there is clear evidence that the reservoir is the soil

become air-borne. As a consequence, infection of laboratory workers is not uncommon.

Haplosporangiosis caused by a rather similar fungus, *Haplosporangium parvum*, affords an interesting parallel to coccidioidomycosis. This pulmonary infection is widespread among rodents and other soil-burrowing mammals in Canada and other parts of North America outside the range of coccidioidomycosis and also in Europe where it has recently been recognized affecting moles in

dust and the incidence of the infection in troops stationed during the last war in areas where the fungus is endemic was reduced by grassing down air fields and by the application of oil sprays to dusty roads.

Another major mycosis of the United States is histoplasmosis (*Histoplasma capsulatum*) which in contrast to coccidioidomycosis is endemic in the central Mississippi Valley and the Ohio Valley.

nose which when examined microscopically are found to contain many large sporangium-like bodies. Instances have been noted of

among the factors which may determine infection Dispersal of [illegible]

[illegible]

mycoses showing this pattern are common endogenous infections [illegible]

[illegible]

particular fungi Sometimes the behaviour of the host may play a part It is considerations such as these that should provide valuable pointers for the experimental solution of some of the many epidemiological problems on the dispersal of mycoses which still require elucidation.

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THE DISPERSAL OF BACTERIAL PLANT PATHOGENS

By

J. E. CROSSE

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PLANT pathogenic bacteria are dispersed by a variety of agencies including man, insects, wind and rain. In some diseases all, or nearly all, of these are involved at some stage or other and transmission is a complicated process. The proper evaluation of the different methods of spread, one in relation to another, is therefore of considerable importance in the formulation of effective control measures For this reason it is proposed to exceed the terms of reference of this particular section of the symposium, and discuss the problem of transmission as a whole. This, it is felt, will provide the best basis for discussion. It is convenient to deal with this subject under two general headings, namely (1) the source and transmission of (primary) infection into new crops, and (2) the

In plant diseases the main sources of primary infection are the various overwintering forms adopted by the pathogens during the temporary absence of a susceptible host or host organs, or on the advent of conditions unfavourable for the establishment and maintenance of disease The majority of plant pathogenic bacteria form no resting spores or structures comparable to those of the

fruits, *X. pruni* and *Pseudomonas mors-prunorum*, have become adapted to a complete pathogenic cycle in which a foliar stage alternates with an active winter stage in the stems or branches Cyclical infection is occasionally a feature of annual legumes, the

pathogen, e g *Ps pisi* and *Ps. phaseolicola* invading the testa of the seed, and even, *in the case of the latter species, the embryo itself* (Pugsley, 1936) In most annual plants, however, the bacteria survive non-pathogenically on or inside the testa; they are apparently no different in this respect from saprophytic bacteria occurring ... The extent

... ted by

... ito the crop with seed, tubers, cuttings and nursery trees, etc, and in the same way bacteria have been transmitted to hitherto disease-free ...

Ps. phaseolicola, the cause of halo-blight of bean, was introduced to this host in the U.S A from the kudza-vine, a legume imported into that country from Asia. Similarly, sugar cane, although not a ...

A few species, e g *X. campestris*, *X. malvacearum* and *C. michiganense*, may occasionally survive the interval between crops in diseased plant residues in or on the soil; *Ps phaseolicola*, *C sepedonicum*, *E tracheiphila*, *X. stewarti* and others have been reported by various observers not to do so The last two species are known to over-winter within the body of hibernating adult beetles which carry and inoculate them into succeeding crops (Rand and Cash, 1920, Poos and Elliott, 1936).

Under experimental conditions *X. vasculorum* (North, 1935), *X juglandis* (Smith, 1921) and other species declined rapidly in unsterile soils reaching extinction within a period of weeks or days. To what extent these results reflected the sensitivity of the isolation methods employed is not clear Evidence of this sort for the non-survival of *X citri* (Fulton, 1920), however, appears confirmed by the events, this organism having been eradicated from certain citrus-growing areas of the U S A by the systematic destruction of diseased plants

The disappearance of short-lived species from soils has been variously attributed to the bacteriophage and to the antagonism of the soil microflora. Patrick (1954) isolated a great number of antagonistic organisms from soils, mostly actinomycetes and [illegible]

them, e g *A* [illegible]
range, the lat [illegible]
many weeds ([illegible]
specialization [illegible]
(Garrett, 194 [illegible]
in the soil. [illegible]

[illegible]

surfaces of plants. For these reasons it is most improbable that

the wind dissemination of free bacteria comparable to that of fungal spores is important in the spread of disease. These points will be referred to later in connection with rain.

The vital role of rain in the numerous leaf spot and similar

malvacearum). His observations have been since confirmed for many other diseases. Despite its importance, comparatively little is known about the physical aspects of splash dispersal In the

rain drops, however, dispersal in the field is almost certainly the result of a chain of very short range transmissions and probably depends amongst other things on the frequency, intensity, and duration of the rain In addition to its dispersive activity rain functions in two other directions It provides first for the mobilization of inoculum, this is normally formed within the plant and reaches the surface in the form of slime or ooze where it becomes hardened and fixed under dry conditions. Rain also affects the entrance of bacteria through wounds and natural openings. Thus in conditions leading to epidemic wildfire of tobacco, water penetrates the stomata causing temporary water-congestion of the intercellular spaces (Clayton, 1936) Bacteria are either carried in during this process or enter in the continuous liquid passage thus provided between the interior and exterior of the leaf (Diachun *et al*., 1942). Again, in the bacterial canker of stone-fruits caused by *Ps mors-prunorum*, infection drops are projected from bacteria-laden leaf surfaces and arrive on the leaf scars where they are sucked into the xylem elements of the leaf traces by the tension in the vascular system of the tree (Crosse, 1951) For infection of this kind, free water is essential.

relation to other methods of spread, however, may have been over-emphasized. A few special associations between bacteria and insects are known, two of which, namely *E. tracheiphila* and *X.*

stewartii with phytophagous beetles, have already been noted. For *E. tracheiphila* the association appears obligate since no other methods of overwintering or transmission are known. In addition

[illegible]

nothing so far to suggest they are of any major importance in the spread of the disease. There is increasing evidence that nematodes are important in some diseases The hyperplastic "cauliflower" disease of strawberry caused by *C fascians* for example, occurs only in plants infested with the leaf and bud nematodes, *Aphelenchoides*

[illegible]

In addition to the main dispersal methods described above bacteria may also be accidentally spread by a variety of cultural practices, e g in irrigation water, etc and on implements and knives A good example of the latter is provided by the vascular infecting *Corynebacterium* spp Thus *C insidiosum*, causing a wilt of alfalfa, is spread by cutting blades during mowing and *C. poin-*

[illegible]

not been overwhelmingly successful as plant pathogens In conclusion therefore it is proposed to examine briefly the bearing disease transmission may have had on the evolution of pathogenic forms

[illegible]

already been noted Here, according to Burkholder (1948) they have attained a dependency that leaves them vulnerable when this association fails ".

Unlike the fungi the bacteria are not adapted to wind dissemination nor have they developed really efficient insect vector relationships

the wind dissemination of free bacteria comparable to that of fungal spores is important in the spread of disease. These points will be referred to later in connection with rain.

The vital role of rain in the numerous leaf spot and similar

Carsner, 1918), but the main effect of rain is the splash dispersal of *inoculum through the air.* The importance of this, especially when rain is driven by winds, was first clearly recognized by Faulwetter (1917 a) during studies of the angular leaf spot of cotton (*X. malvacearum*). His observations have been since confirmed for many other diseases. Despite its importance, comparatively little is known about the physical aspects of splash dispersal. In the

result of a chain of very short range transmissions and probably depends amongst other things on the frequency, intensity, and duration of the rain In addition to its dispersive activity rain functions in two other directions. It provides first for the mobilization of inoculum; this is normally formed within the plant and reaches the surface in the form of slime or ooze where it becomes hardened and fixed under dry conditions. Rain also affects the entrance of bacteria through wounds and natural openings. Thus in conditions leading to epidemic wildfire of tobacco, water penetrates the stomata causing temporary water-congestion of the intercellular spaces (Clayton, 1936) Bacteria are either carried in during this process or enter in the continuous liquid passage thus provided between the interior and exterior of the leaf (Diachun *et al*, 1942) Again, in the bacterial canker of stone-fruits caused by *Ps. mors-prunorum*, infection drops are projected from bacteria-laden leaf

THE SOIL AS A RESERVOIR OF PATHOGENIC MICRO-ORGANISMS

By

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THE soil can be all things to all men To the pathologist, it may be merely a reservoir of pathogenic micro-organisms, though as a human animal he must himself subsist, directly or indirectly, upon its products As a thinking animal, he will be wise to learn more about the soil than may at first seem strictly necessary for the solu- [illegible]

anatomy and all the other branches of medical science, unless he [illegible]

generalizations from his own personal experience for the benefit [illegible]

tolerably well acquainted with the saprophytic behaviour in pure culture of most of the important parasites known to us Unfortunately, however, the requirements and behaviour of an organism in pure culture are not a reliable guide to its saprophytic behaviour in

comparable to those of the viruses. Both these are considerable disadvantages in plant diseases where, by the nature of the host, the onus of spread rests with the pathogen. Short range splash dispersal may be extremely effective under agricultural conditions, but in natural vegetation, where pathogenic forms probably first evolved, its limitations are obvious

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A similar problem is presented by *Cercosporella herpotrichoides*, causing the eyespot disease of cereals (Macer, 1955). The most likely explanation at present available suggests that the parasitic fungus, which becomes firmly established in the host tissues from the outset of occupation, is able to prevent massive saprophytic

trichoides form, so far as is known, such specialized resting organs as resting spores or sclerotia, which account for the prolonged

elsewhere our present knowledge of the dormancy of root-infecting

habiting fungi (Garrett, 1950) The soil-inhabiting fungi are to be distinguished by their ability to exist independently of their host plants as free-living saprophytes in the soil. The root-inhabiting fungi are more specialized parasites that seem to have lost the power of independent life as competitive saprophytes, and their saprophytic behaviour is more or less confined to saprophytic survival

matically ensures that a parasite will, at all times and in all places,

[1] We are indebted to Dr P W Brian, Akers Research Laboratories, Welwyn, for this information.

the soil, where success of the organism in the struggle for survival is governed not merely by its intrinsic saprophytic capacities in the utilization of various substrates but also, and more directly, by its capacity for competitive colonization of substrates in the presence of other micro-organisms. The parasitic behaviour of most of the important plant and animal parasites has been much studied and considerably elucidated; our ignorance of their saprophytic behaviour in nature stands consequently in the sharper contrast. It

demiology as the saprophytic life of parasites in the absence of their hosts It is now for the microbiologist to redress this balance, inasmuch as the micro-organism rather than the host should be the centre of interest for him, as Burnet (1953) has indeed argued with an eloquence and an erudition that I cannot hope to command.

In our work upon the root-infecting fungi, we have sharply distinguished between two kinds of saprophytic behaviour in a state of nature. saprophytic survival and saprophytic colonization. All the fungi that we have so far investigated show considerable, and fairly comparable, powers of saprophytic survival; ability for saprophytic colonization, however, varies widely, and seems to be inversely correlated with the degree of parasitic specialization.

host plant dies, the root-infecting fungus continues to live as a

saprophytic competition is not finally decided at the surface of the substrate, but progressively shifts with penetration of the competing organisms deeper and deeper into the substrate

laboratory, frequently provide a firmer foundation for further advance than data obtained under the more restricted conditions of precise experimentation

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successfully infect its host plant, the outcome of saprophytic competition, like that of parasitic invasion, is influenced by the inoculum potential of the organism concerned, by the strength of the opposition (other micro-organisms in one instance and host resistance in the other) and by the over-all effect of the environment. It has been

the host-parasite relationship, and that the loss of this characteristic by specialized parasites is not merely an incidental loss of an inessential attribute. Our studies of the root-infecting fungi have therefore suggested that the obligate parasite is merely the final term of a series showing progressively increasing losses of competitive saprophytic ability.

We now have convincing evidence that a number of root-infecting fungi can colonize dead plant tissue as competitive saprophytes; it

inoculum of each fungus was mixed in a series of dilutions with unsterilized soil, which provided the competing saprophytic micro-organisms In these inoculum/soil mixtures were then buried the sterilized pieces of wheat stem tissue that were used as test substrates for saprophytic colonization by the inoculant fungus. With all fungi, the percentage of wheat stem pieces saprophytically colonized by the inoculant fungus decreased with decreasing propor-

FUNGAL DISEASES OF PLANKTON ALGAE

By

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MANY freshwater algae are parasitized by fungi belonging to the Phycomycetes. The groups mainly concerned are the uniflagellate Chytridiales and simple biflagellate forms. Those infecting planktonic freshwater algae have received attention in recent years (Canter, 1950, 1951, 1954, Canter and Lund 1948, 1951, 1953) [illegible] specificity. Though the life-histories of chytrids are diverse in detail, in broad outline most show certain features in common. Asexual reproduction is mainly by flagellate spores, several being produced in a sporangium. These zoospores are almost always globose, small (*circa* 2–5 μ diameter) with a long flagellum which propels the spore from the rear. Asexual or sexual resting spores are also produced by many chytrids. Infection of an algal cell by a single chytrid almost invariably leads to its death even though the fungus does not complete its development, as, for example, if it is itself infected by a parasite (hyperparasite).

A very common feature of parasitism by chytrids is that over a large part of the year but few of the host population are infected. Sometimes, however, the fungi multiply rapidly, faster than the algae, so that the infection reaches epidemic proportions with a consequent decrease in the algal population. As an arbitrary lower limit for epidemics may be taken the point at which one quarter of the host population is infected, this corresponds roughly to the level at which the algal population begins to decrease. The course of epidemics usually follows the same lines. At first there is an increase mainly in [illegible]
on the algal cel [illegible]
sporangia in the [illegible]
dying sooner or [illegible]
of encysted zoo[illegible] small while many dead algal
cells bear the empty cases of dehisced [illegible]

in turbulent motion so that the host plants are distributed at random. It is true that, under conditions of thermal stratification, the

is commonly of the order of 150 μ and since the height of the helix is only about 10 μ, it may be looked upon as a flat stellate colony. The cells themselves are clearly *not far* apart even at their free outer ends (*circa* 50–100 μ apart) and a zoospore should be easily able to swim from one cell to another, particularly since the water between the cells is unlikely to be in turbulent motion. Epidemics could, therefore, arise rapidly by an increase in the number of the cells infected in colonies already bearing a single chytrid. If each of these cells produced 10 zoospores and half of these made contact with other cells in the same colony infection of the population as a whole could rise from 1 per cent, which is about the average level of infection between epidemics, to 30 per cent by the production of two new generations of parasites. However, observation shows that

arise from their germination in the space of a fortnight, as it does. Nevertheless, they may play a part over longer periods of time (see later).

[illegible] what this host population density should be. We can, however,

causes of epidemics clear, and though attempts have been made no successful experimental work has been done. The algal hosts can nearly all be grown in culture, but the parasites die rapidly. Even in the most severe epidemic, it is only necessary to place the algae in any container in their natural water or any culture solution to free them of parasites in a short time. It is, therefore, only possible to theorize about the causes of epidemics. For this purpose I shall take the parasitism of the diatom *Asterionella formosa* Hass by chytrids belonging to the genus *Rhizophidium* as an example The ecology of this diatom is relatively well-known (Canter and Lund 1948, 1951, Lund 1949, 1950) and its parasitism has been followed in nature in certain lakes at weekly or lesser intervals for some nine years. The lakes concerned are Windermere, Blelham Tarn and Esthwaite Water, all in the same drainage area in the English Lake District. The outflow of Blelham Tarn passes into the north basin, and of Esthwaite Water into the south basin, of Windermere The two basins of Windermere may be considered as separate bodies of water since there is between them an area of shallow water in which lies a group of islands. The north basin, then, forms the main inflow of the south basin but a small amount of water from the latter may pass up into the former in the surface drift if southerly winds prevail, as they very frequently do. The parasites are not killed to any significant extent in passing down the streams connecting Blelham Tarn and Esthwaite Water to Windermere. Thus, the *Asterionella* population in the north basin of Windermere may be infected by parasites from Blelham Tarn and via the surface drift by those from the south basin which, in their turn, may include specimens from Esthwaite Water. Similarly, the *Asterionella* in [illegible] be infected by parasites from the other three

[illegible] bodies of water

indeed in all but Blelham Tarn the spring maxima are closely similar. The frequency of chytrid epidemics decreases in the order Esthwaite Water, Blelham Tarn, Windermere, south basin, and Windermere, north basin. This order agrees approximately with the

is more frequently above the minimum spatial limit (*circa* one colony per c c) than in the others Indeed the ratio of the number of epidemics between say Esthwaite Water and Windermere north basin is almost exactly the same as the ratio of the lengths of time there are one or more colonies of *Asterionella* per c.c. in the water It is also possible to explain the fact that epidemics arise at different times in bodies of water flowing into one another without reference to possible differences in the substances in their waters We can

very infrequent, as sometimes happens, particularly in other lakes, the parasites may diminish to an even greater extent As the

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Assuming this, at a mean density of one colony ... given volume 2 per cent of the cubic centimetres can be expected to contain four colonies; *for a mean density of four colonies per c.c.*, 57 per cent of the cubic centimetres can be expected to contain four or more colonies. We may presume that it is the proportion of a host population lying within a certain minimum distance apart which determines whether or not an epidemic may arise. Since the greatest *mean distance apart of the host colonies in the recorded epidemics* is of the order of one centimetre, it seems very probable that they can only occur if these host colonies are near enough to one another to ensure that the water movements are not so great as to very

the fact that in the more

BACTERIA OF VETERINARY IMPORTANCE AND THEIR TRANSMISSION BY NON-BIOLOGICAL AGENCIES

By

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The methods of breeding, housing and feeding domesticated animals vary from species to species and differ according to custom and in accordance with geographical and climatic conditions In temperate zones, cattle and pigs are housed and sheep are allowed greater freedom, whereas, in tropical countries, cattle have a [illegible]

[illegible]

bacteria, such as those belonging to the acid fast group, will withstand extremes of temperature for many months and spores from the *Bacillus* and *Clostridium* groups may survive for years outside the animal body. The spread of these bacteria by non-biological agencies is therefore conditioned by the survival of the bacteria and by the environmental conditions of the host These variations suggest that we should consider a few of the bacterial diseases of animals and thereby learn something of the importance of non-biological agencies which spread infectious diseases to domesticated animals.

Infection takes place by the alimentary tract and the bacilli are [illegible]

unopened carcass, but when the bacteria are exposed to atmospheric conditions spores are produced and these are resistant and may remain alive in or on infected soil for many, many years Animals may therefore be infected by feeding on contaminated [illegible]

Britain is much higher during the winter months of the year because most of the outbreaks are associated with feeding imported, infected foods; the cases are sporadic and there is no epidemic. The disease is therefore not only more common during winter months when artificial foodstuffs are used but is clearly more frequently observed amongst cattle which are fed on imported foodstuffs than amongst those cattle and sheep which are fed in a different manner

Infections caused by Members of the Clostridium Group

The members of the *Clostridium* group are spore-bearing anaerobic organisms and many of them infect domesticated animals. The reservoir of infection is the soil and the intestinal canal of man and animals. Tetanus, black-quarter, braxy, black disease, lamb dysentery and botulism are examples of diseases associated with this group of organisms.

[illegible]

are capable of causing disease in sheep whereas the first form more frequently causes disease in cattle

The disease affects young cows particularly and there is a long period of incubation of one and one-half to two years and latent infection is *apparently quite common; Johne's bacilli may be* isolated from a proportion of healthy cattle. In Scotland, in Iceland and in some other countries the disease affects sheep. In both species of animal infection occurs through ingesting fodder or drinking water that has been soiled with the faeces of infected animals.

In some experiments, made about ten years ago in Berkshire, infected faeces were placed in shallow ponds which were guarded from infection from animals by surrounding them with mesh wire. Cultures were made at monthly intervals and in spite of the fact that varying conditions of weather occurred, such as rain and sunshine, snow and frost, it was possible to recover the bacteria for upwards of eight months afterwards. These faeces were from an infected cow and it is therefore easy to see how this disease is spread by the faecal contamination of water, of feeding materials and of pasture land by infected animals Pasture land and stagnant water may remain dangerous, particularly for young animals, for many months

The climatic and other conditions influence events, and it is interesting to ... Johne's
disease in shee
and were dist
different farms. Five or six years later, Johne's disease developed on those farms and has since spread through the country. There ... among the sheep in the country of

closely together for some of the winter months; the spread of the *infection* would therefore take place very readily under these conditions.

Anthrax

Anthrax is primarily a disease of animals and is widespread in ... is endemic the

of some of these diseases Tetanus, black-quarter, black disease, braxy and lamb dysentery have this peculiar geographical distribution and the longevity of the spores in the soil is one of the facts associated with this patchy distribution.

Swine Erysipelas

Swine erysipelas is caused by *Erysipelothrix rhusiopathiae*, which

have some influence in determining the period of longevity for it apparently lives much longer in putrefying than in smoked or salted pork and longer in distilled water than in ordinary water The danger of introducing susceptible pigs into an area or house in

subsequently driven through the dip will develop an infection with this organism This demonstrates the spread of *E rhusiopathiae* infection by water as well as by the contamination of soil.

Caseous Lymphadenitis and Ulcerative Lymphangitis

Corynebacterium ovis is the cause of a caseous lymphadenitis in

Braxy is the name given to a disease which occurs in sheep and occasionally in cattle and is caused by *Clostridium septique* This organism is found in faeces and in soil. The infection is associated with invasion of the wall of the fourth stomach of the sheep and this occurs especially after cold and frosty nights; there is thus the suggestion that the subsidiary factor is a climatic condition

Black disease is another disease of sheep and associated with infection with *Clostridium oedematiens Clostridium oedematiens* is a *spore-bearing rod which may lie latent in the tissues of sheep and in* soil; it may be stirred into activity by wandering immature flukes (*Fasciola hepatica*) The infectious hepatitis which develops is due to the activity of *Clostridium oedematiens* which may be in the soil but also lies latent awaiting this activation by some subsidiary factor, which in this case is the liver fluke.

Lamb dysentery is associated with one of the types of *Clostridium welchii* which sporulates rather rarely but nevertheless is found in the soil, in milk, in dust and in the intestinal canal of man and animals Type B is associated with lamb dysentery and may be found on the teats and mammary glands of the mothers, and the lamb becomes infected during the suckling period and develops the disease within a day or so of birth

Botulism occurs in animals as well as in man and although technically *Cl botulinum* is a saprophyte, it produces its toxin in foodstuffs before ingestion. The spores are found in soil and many cases of botulism occur in domesticated animals throughout the world, the incidence is associated with the spoiled foodstuffs with which they are fed Wild duck may feed upon certain marshy lands where the spores of *Clostridium botulinum* have been lying latent, and under suitable conditions of growth and if there is little or no competition from other organisms they develop and produce toxin in the marshy vegetation, the ducks which feed there develop botulism. Other forms of botulism may occur when cattle, sheep or goats feed upon *the bones of animals which have died and have been left to lie on the* surface of the ground This abnormal craving for bones by herbivora occurs when the cattle or other animals are short of phosphorus because of a deficiency in the soil and vegetation In order to overcome this deficiency they have a craving for chewing the bones of dead animals and if these animals are infected with *Clostridium*

the tissues, but in addition these organisms remain alive as spores in the soil in certain areas, and this influences the regional distribution

DISPERSAL OF PATHOGENIC AMOEBAE

By

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Information concerning the dispersal of parasitic amoebae is

hatches from the cyst and commences a further period of growth
The dispersal of pathogenic amoebae is described below, *E histolytica* and *E coli* being treated separately.

Entamoeba histolytica

Life cycle. Cysts discharged with the stools are swallowed by a suitable host and hatch in the small and large intestine After completion of a series of nuclear divisions following excystment,

formed until symptoms subside Under certain conditions, as yet

are instantly killed by drying
Cysts in the faeces remain viable for at least two weeks when kept at room temperature, but for as long as two months if kept in the

[illegible]

which were ideal for the infection and development of an ulcerative lymphangitis of the legs caused by *C. ovis*.

[illegible]

Summary

It is clear therefore that the importance of soil, water and air as a means of spread of bacterial infection in domesticated animals is dependent very largely upon the contamination of the medium from infective animals. Many diseases spread by air are more or less direct by droplet infection; many of those in which water or soil play their part are associated with heavy contamination of the [illegible]

infection if large areas of soil or large tracts of water are infective.

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a recent survey of a section of the British population showed that the incidence of *E. histolytica* infection was 1·6 per cent whereas that of *E. coli* was 24 7 per cent.

Experiments on the transmission to man have recently been carried out with this parasite Cysts of *E. coli* were given in the drinking water and in capsules to human volunteers The results showed that the ingestion of one cyst could give rise to a heavy infection The experiments with cysts in the drinking water showed this was the most effective route as all volunteers were infected. Experiments on transmission by flies were of limited success and only occurred where the fly contact with cysts and food was most intimate.

The monkey (many species) is an alternative host for *E. coli*, though as described for *E. histolytica*, transmission to man is unlikely. The rat is not infected with *E coli*.

Other entamoebae

The life cycle of *Entamoeba invadens* resembles that of *E histolytica*, but differs from it in certain features which affect its method of transmission *E. invadens* infects reptiles, mainly snakes, and differs from *E histolytica* in that it is invariably pathogenic. In

[illegible]

parasite to establish a new infection

Although cysts may also be passed in the faeces of the snakes, the chances of dispersal by this route are reduced, owing to long periods between defaecation by these animals The encystation of tissue-dwelling amoebae represents an adaptation to the habits of the reptilian host

In addition to the three species described above, there are many species of *Entamoeba* and other genera which infect representatives of almost the whole animal kingdom The efficiency of their dispersal can be attributed solely to the vast numbers of cysts produced.

References

[illegible] *Entamoeba* [illegible] *Proc zool* [illegible]

[illegible] *Protozoology*, [illegible]

refrigerator. In water or culture, cysts remain viable for about a month at room temperature, though when kept in culture at 4° C. they usually survive for three months.

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belong to a free-living coprophilic species, which is harmless to man, though morphologically indistinguishable from the "dysentery amoeba".

Transmission. Transmission of the cysts occurs if they can reach the water supply either through primitive arrangements for disposal of faeces or by a breakdown of the plumbing system which will allow contamination by sewage, or by contamination of food or drink by infected food-handlers, flies or cockroaches. Cysts have been observed in flies and cockroaches, and experiments have shown that viable cysts are passed for as long as 31 hours in the faeces of flies (*Musca domestica* and others) and 48 hours in the case of

amoeba is transmitted from one monkey to another, it is not likely that transmission to man is frequent owing to lack of contact

wild rats is low and experiments have shown that cysts are not formed in very large numbers. Rats also probably acquire their infection from man, therefore they may be regarded as incidental hosts

Entamoeba coli

The above remarks concerning the life history, viability and transmission of *E histolytica* also apply to the non-pathogenic human parasite *E. coli* with one important difference. This is that the cysts of *E. coli* are not killed by drying, and distribution may also be air-borne, though this has not yet been proven by experiment. This difference is reflected in the higher incidence of infection; thus

FACTORS AFFECTING THE TRANSMISSION OF COCCIDIA AND THE DEVELOPMENT OF DISEASE IN FOWLS

By

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THE coccidia are members of the protozoan Class Sporozoa and are widely distributed parasites of invertebrates and vertebrates They are usually parasites of the main intestinal tract but a few species occur in other sites, e.g *Eimeria stiedae*, which passes its complete life history in the liver of the rabbit, and *E truncata* which passes at least the later stages of its life history in the kidney of the goose. The coccidia usually live on reasonably balanced terms with their hosts but here consideration is give to some of the factors that may disturb this balance

The Life cycle

Two genera of coccidia, *Eimeria* and *Isospora*, contain species which may cause disease in domesticated mammals and birds The present review is devoted to those *Eimeria* species which inhabit the intestinal tract of domestic fowls The life cycle, which is direct, consists of one or more generations of schizogony followed by

sporulation whereas unsporulated and sporulated oocysts may be killed after more or less prolonged exposure to exceedingly low or high temperatures.

Under natural conditions it seems probable that although extremes of temperature may destroy oocysts it is the influence of low rather than of *extremely* low temperatures that produces the most far reaching effects. These low temperatures do not kill oocysts but merely prevent the freshly-passed oocysts from sporulating, or they may markedly reduce the rate at which sporulation proceeds If coccidia-free chickens are put out onto ground at the end of

viable oocysts are introduced into their environment Should the

exposed or sheltered sites

Temperature, desiccation, available oxygen, bacterial and fungal

develop and form large second generation schizonts which again produce merozoites. The fate of the second generation merozoites may differ in that some of them may initiate a third generation of schizogony whereas most of them differentiate into male and female gametocytes. The micro- and macrogametes derived from the gametocytes combine to form oocysts. The whole cycle from ingestion of oocyst to production of new ones may be completed in four to seven days according to the species.

Factors influencing transmission

Transmission is effected by the sporulated oocyst. The process of sporulation is controlled by the conditions of the environment into which the unsporulated oocyst is passed. There is evidence that bacterial and fungal action is detrimental to oocysts, but to what extent oocysts are destroyed in this way in nature is not known. If the effect of bacteria or fungi is ignored then the principal factors affecting sporulation or viability are related to the presence or absence of oxygen or moisture and to average or extremes of temperature Both unsporulated and sporulated oocysts quickly succumb when denied either oxygen or moisture. They are highly tolerant of the average high and low temperatures encountered in [illegible]

than on its capacity to destroy them The optimum temperature [illegible]

[illegible]

these oocysts examined at different intervals showed that by the end of the second day most of the oocysts held at 37°C had become infective but that no sporulation had occurred in oocysts held at 8°C. for eight weeks However, a small percentage of the oocysts [illegible]

[illegible] ture of 45°C. were killed in 24 hours, as were those stored at —12°C for seven days (Edgar, 1954). Temperatures at either extreme inhibit

on the ability of the species to produce oocysts and the degree to which the host is susceptible.

Greater yields of oocysts may be obtained from light than from heavy infections. Blackett and Bliznick (1952) have shown that the oocyst-productivity (or reproductive potential) differs from one

infection can produce under any circumstances is considered *E. necatrix* proved to be the least prolific of all the species occurring in the fowl. In the light of these findings it may be assumed that there is a rapid increase in the accumulation of oocysts when susceptible chickens are introduced into an environment populated by small numbers of viable oocysts of *E. tenella* or *E. brunetti* which have high reproductive potentials in light infections. The low oocyst

caecal coccidiosis may develop by the fourth day after initial in-

of age and are more resistant at two weeks of age than at any other period during the first six weeks of life.

Another controlling factor in the development of disease is probably that of age of oocysts. The activity of cultures of *E. tenella* oocysts is reduced

tenella may also produce infections in other avian hosts. These

... relative pathogenicity, some appear to

more commonly encountered. Immunity to the pathogenic species develops quite readily but there is no cross-immunity between species, a character often used to determine specific identity Immunity is

by such fowls and these oocysts will become infective to other fowls if or when the environmental factors favour sporulation. Therefore, *oocysts derived from immune carrier fowls may prove a hazard to* susceptible fowls put into the same quarters

Factors influencing the development of disease

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doses of oocysts of *E. acervulina*, *E mitis* or *E. praecox*. Much work remains to be done on the pathogenicity of species and the reasons underlying it, differences in pathogenicity may be related to the depth to which the parasites penetrate the tissues, to the ... and dimensions *of the second generation schizonts* in some

s, the

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important part in deciding whether a susceptible host introduced into that environment may remain susceptible, or become immune or diseased.

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[illegible]

immunogenicity. The disease-producing potentialities of the coccidia are dependent on the inherent pathogenicity of the species, the numbers of oocysts that are produced by such species and the susceptibility of the fowl population in contact with them Fowls picking up few oocysts will gain some resistance to heavier subsequent infections but, up to a point, the greater the numbers of oocysts ingested the more solid is the resistance developed It is no uncommon experience, however, to encounter some deterioration in condition, or even deaths, among individuals in groups of fowls before other individuals within the same groups have developed an immunity. Small ground infections give rise to large ones and fowls exposed to them may either pick up gradually increasing numbers of oocysts and thereby become immune, or, alternatively, may pick up excessively large numbers at one time and so develop disease before any solid immunity has developed In *E. necatrix* infections the low oocyst potential is not sufficient to stimulate immune responses in young

production of *E necatrix* and the consequent intake of only lightly

are ingested later, to reach maturity in the intestine while the older worms are still there, and so on, until massive infestations are

exogenous stages of parasites are passed into an environment outside a host animal the conditions prevailing in that environment play an

THE TRANSMISSION OF HELMINTHS OF VETERINARY IMPORTANCE

By

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PERHAPS it is part of the general scheme for the stimulation of mental

larly incongruous about these instructions

host to parasite and of parasite to host with particular reference to the non-biological agencies with which my section is asked to deal. The outstanding peculiarity of the parasitic helminths is that, with very rare exceptions, they do not give rise to successive generations

infective material is exposed under natural conditions, it is, neverthe-

infective larvae develop in large numbers. If this ground is ploughed and worked with harrows, it may still further assist, as the larvae through their own activities quickly regain the surface of the soil

danger is linked with the type of crop rotation that introduces occasional "catch crops" of green food such as rape or vetches interposed between two successive crops of corn.

A further example that might be mentioned concerns the lush pastures of our modern grass land, brought about by the specially selected grasses and clovers, and the extensive use of artificial manures; these pastures add to the dangers in two ways, firstly by leading to greater concentration of the grazing animals (as has been shown there is a tendency for the rate of infestation with parasitic worms to increase as the square of the numbers of grazing

This acquisition of resistance before the host reaches maturity is again largely a matter of numbers of parasites. The dose must be adequate to stimulate the response. As yet, very little is known about the mechanism concerned but it seems to be clear that both age and experience of infection are necessary for its development and that the rate of acquisition of the parasites is of importance. If some 50,000 *Trichostrongylus axei* were to be administered to a susceptible lamb over a period of a few days, the lamb would in all probability develop severe disease and die. If, however, the dosage were to be spread over several weeks, the lamb would have acquired a resistance as a result of the early infestation, and those larvae administered

greatest importance to the increase of the infective potential. In

for defaecation and cattle will avoid the grass near to deposits of cattle faeces for weeks.

These points, however, come under the heading of biological

and so to bring about a heavier infestation of the pastures. A great deal of information on degrees of temperature and of moisture associated with minimum or optimum development has been collected in laboratories. Although much of this is not directly applicable to occurrences in the field, in that we have little information on the degrees of temperature or of moisture to which the

mass development only when the snow cleared away, with the approach of spring, so that a large proportion of the winter's accumulation of eggs reached the infective stage all at once.

This same accumulation of potential infection also appears to operate in connection with the severe springtime outbreaks of [illegible]

[illegible] preceding generation had occupied during the previous year. The precise reasons for the increased prevalence of this condition at the present time are not yet to hand, but doubtless refer to some feature of modern grassland management

As a final example, I might refer to a tentative conclusion of Dr. Ollerenshaw who has been working in my department on the ecology of *Limnaea truncatula* and its association with *Fasciola hepatica.* Having ascertained the minimal temperature requirement for the larval fluke within the snail, the rates of development at various [illegible]

[illegible] emerge during the month of July.

At this point it is convenient to notice the effect of drought in stepping up the intake of infective larvae In the example of the liver fluke, it concerns the accessibility of fluke-infested herbage to the grazing animals So long as the shallow ditches and hollows [illegible]

[illegible] may be a very high concentration of encysted cercariae in such [illegible]

[illegible] small areas of pasture near to watering places, or in damp depressions in the ground. The same effect of local concentration is also brought about by the improvement of small areas of pasture on extensive hill grazings or on large prairies (as in North America) where the overall relationship of one sheep to four acres of ground may be virtually changed into a local concentration of some fifteen

the month of August, at Washington, D.C. After allowing a suitable period of time for the development of the infective larvae, he recovered one larva for every 506 eggs in faeces in the grass, but only one larva from approximately every 660,000 eggs in faeces on the plots that were free from vegetation.

Resting stages of helminths

must possess an adequate power of resistance, in order to enable them to await the arrival of that host In general, these resting stages are either eggs containing infective larvae, or the infective larvae enclosed in loose skins that have not been completely cast off at the last ecdysis A few examples are known, however, where the embryonated egg, just prior to the liberation of the first-stage larva, is exceedingly resistant to adverse conditions.

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is retained in the faecal mass for at least some of the embryos to *reach the point of full development before absence of moisture puts* a stop to further development. Those eggs that hatch come to
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eggs which
So long,
however, as the *infected animals continue to graze on that ground*, under those conditions, the partial development and halting at the particularly resistant stage will continue for some of the eggs until a very large number of embryonated eggs accumulate and the infection potential on the ground is very high. A change to wet weather then enables *all of these accumulated embryos to proceed* with their development and in the course of a few days a very large number of the infective larvae appear and endanger the health of

Nematodirus
Moscow to the accumulation of resistant eggs which began their

mass development only when the snow cleared away, with the approach of spring, so that a large proportion of the winter's accumulation of eggs reached the infective stage all at once.

This same accumulation of potential infection also appears to operate in connection with the severe springtime outbreaks of nematodiriasis in that the eggs of this genus mature slowly and the condition requisite for development are such that a great concentration of larvae appears on the herbage during the spring, and the lambs, which are too young to have developed a resistance against this species, suffer severely when placed on pastures which the preceding generation had occupied during the previous year. The precise reasons for the increased prevalence of this condition at the present time are not yet to hand, but doubtless refer to some feature of modern grassland management

As a final example, I might refer to a tentative conclusion of Dr Ollerenshaw who has been working in my department on the ecology of *Limnaea truncatula* and its association with *Fasciola hepatica* Having ascertained the minimal temperature requirement for the larval fluke within the snail, the rates of development at various [illegible] emerge during the month of July.

[illegible] in the ground are inundated, they are suited only to water creatures among which may be numbered the intermediate host that thrives and gives out its numerous cercariae. A period of drought, perhaps accompanied by a shortage of pasture herbage, occurring in the latter part of the summer, then results in the grazing animals going on to parts that were flooded and eating the infected grass As there may be a very high concentration of encysted cercariae in such [illegible] small areas of pasture near to watering places, or in damp depressions in the ground The same effect of local concentration is also brought about by the improvement of small areas of pasture on extensive hill grazings or on large prairies (as in North America) where the overall relationship of one sheep to four acres of ground may be virtually changed into a local concentration of some fifteen

or twenty sheep to the acre. Under these conditions it is often necessary to fence the sheep out of the improved ground, in order that helminthic disease may be avoided through controlled grazing.

Elasticity of host-parasite relationship

The relationship of host to parasite, which has evolved along with the evolutionary development of the two species, learning how to live together satisfactorily, is upset as soon as there is an increase in the chances of each egg getting back to the host. A certain very considerable elasticity is, however, provided by the resistance of the host, which is able to develop defence mechanism as it grows towards maturity. These are partly the outcome of changes that are associated with the ageing of the tissues, and partly a response to previous infection with the parasite, i e. there is an "age resistance" and an "acquired resistance", the latter being the more powerful. With all the great improvement of the pastures, the fencing-in of the stock and the very greatly increased concentration of grazing animals, the remarkable thing is that they ever escape disease. Our observations on certain experimental plots showed that ewes may acquire daily some 7,000 infective Trichostrongyle larvae without suffering disease. Even these resistant animals, however, do carry a number of worms and it is not yet possible to explain the mechanism ... to enable it to live

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varying from such extremely remote contact as to endanger the continuity of the parasite species to such overcrowded conditions that the continuity of the host species become endangered from over-parasitism.

daily to the pastures ... resistance In working out some figures recently in my department, a 100-pound sheep was estimated to be passing 4 8 pounds of faeces during each 24 hours and its lamb to be passing 3 pounds On this basis we have observed groups of diseased lambs to be passing up ... per day on to the pasture. Ewes, on the ... instance ... r day was ... 130,000.

carrying 150 larvae per pound, and eating 7 pounds of herbage

area of pasture, then at the same rate of development, but passing 4.8 pounds of faeces, it will be adding 436 larvae daily The average ewe that has been taken as the example, however, eats some 14 pounds of herbage in a day, which, at the rate of 150 larvae per

the pasture

interaction of the several factors some of which (to add to the complexity) operate in two directions at one and the same time; for instance, the factor of short herbage, which tends to increase the rate of the pick-up of larvae, because the sheep bite closer and must

Another gap in our knowledge concerns the precise nature of the microclimate in the field

be the most urgent need at the present time for our better understanding of the non-biological factors concerning helminthic disease.

THE DIRECT TRANSMISSION OF DISEASE BETWEEN TWO ORGANISMS OF THE SAME SPECIES

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ONLY transfer of infection in man will be considered Our concepts of the relative importance of the different routes by which infection is spread within the human community are continually changing This suggests that these concepts are perhaps based on theory rather than on fact However, it is only fair to say that a great deal of experimental work was done in this field, particularly by German

how it maintains its viability and virulence outside the body when spread of infection occurs indirectly, the infecting dose, and, in the case of respiratory infections, the particle size which will allow it to reach the tissue in which infection is to occur The term "infection" must include both latent and overt infection, and the analogy with the iceberg, of which the small visible part represents clinical infection and the submerged bulk bacteriological infection, is relevant

Classification of the modes of spread may be based on

(*a*) route of infection, *e g* respiratory (inhalation), intestinal (ingestion), surface (implantation), or

(*b*) etiological agent, *e g* staphylococcus, haemolytic streptococcus, influenza virus, salmonella, shigella, pyocyanea, etc

The latter classification is probably preferable, for it is fallacious to assume that, for example, different respiratory infections are all spread in the same way, and, of course, infection in any specific disease may be spread in different ways However, it is convenient to discuss here the modes of spread under the categories of respiratory, intestinal and surface

Respiratory Infections

Three main modes of spread of respiratory infection are recognized direct droplet, direct airborne, and indirect airborne.

Direct Droplet

Direct droplet spread requires intimate contact, and it may be difficult to be sure whether the infective material has been directly inhaled from dispersed droplets or whether it has reached the respiratory tract of the susceptible person indirectly through the medium of hands, clothing, and the like.

Direct droplet spread would seem to be the most likely method of transfer for respiratory pathogens that have a poor viability outside the body. Cerebrospinal fever is a good example, since it has been associated particularly with conditions of over-crowding, and Alison Glover's classical work with recruits in barracks during the First World War indicated that by adequate bed-spacing the risk of epidemic spread of this infection could be materially reduced.

Another infection in this category is whooping cough. This is a highly infectious disease for family contacts, in whom the secondary attack rate is around 90 per cent; but it spreads much less easily in hospital wards and day nurseries, where contact is less intimate. In these latter communities, infection may smoulder on over a period of months, in comparison with the explosive outbreaks that frequently follow a primary case of measles.

Studies by the Common Cold Unit at the Harvard Hospital, Salisbury (Lovelock *et al* 1952) have also shown that this common [illegible]

[illegible] material was inoculated intranasally was around 50 per cent.

Direct Airborne

Most of the droplets that are expelled from the mouth during [illegible]

the introduction of a case of measles or chickenpox even although there has been no close contact or other opportunity for the direct transfer of the infective material. It has also been a common experience that "barrier nursing" and cubicle isolation[1] cannot control the spread of these two infections

susceptible persons who were separated from each other by the barrier of a wet blanket. But again the attack rate under these experimental conditions was only around 10 per cent.

Indirect Airborne

other parts of the animal house, and that these animals could be protected from this dust-borne spread of infection by a screen of ultra-violet light There has been considerable controversy as to whether some of the common bacterial respiratory infections in man caused by the haemolytic streptococcus, the pneumococcus, the diphtheria and the tubercle bacillus could be spread by infected dust

As regards streptococcal infection, Hamburger and his colleagues (1945) demonstrated the importance of heavy nasal carriers of the

[1] A cubicle is a single room with a partition which is not a complete structural barrier from the adjacent room

so exposed

It seems likely that the chances of spread of infection by contaminated dust may depend on a number of factors, of which the susceptibility of the respiratory mucosa and the dosage and the degree of desiccation of the infective organism are probably most important. A high rate of secondary streptococcal infection has

high among the children in the oiled ward as in the control ward (Begg *et al.* 1947) The most likely explanation of this paradox was that the load of infection in the second study was very much less than in the earlier investigation, as was shown by air-sampling. There is some indication that secondary streptococcal infection after influenza may also be dust-borne (Cruickshank and Muir 1940) On the other hand, the experience of Rammelkamp and his colleagues indicates that it is much more difficult to induce a *primary* streptococcal infection by infected dust, so that after expulsion the haemolytic streptococcus seems quickly to lose its capacity to initiate infection on healthy tissues.

While nasal carriers of the pneumococcus and diphtheria bacillus are also dangerous and produce gross environmental contamination, there is no clear evidence that dust-borne spread of infection is important in these diseases In the case of tuberculosis, since only very small particles (5μ diameter) can reach the lung parenchyma, and since moist droplets of this size seem seldom to contain tubercle bacilli (Duguid 1946), it is likely that fine dust, for example from contaminated blankets, may be a means of spreading tuberculous infection It would therefore be wise to recommend the wearing of masks by nurses and other attendants during bed-making and dusting in sanatoria. It may be noted here that female laundry workers have

contrast to other food-poisoning pathogens, has its reservoirs in the nose and on the skin, and that septic spots and small infected wounds

its peak
Again,
explosive
outbreaks, and indeed food and water are rarely incriminated as vehicles for the spread of the infection Instead, intimate contact in the home, in nurseries, and in schools, is an important factor in its spread, and contaminated fomites from contaminated hands

An infection of the alimentary tract characterised by the sudden onset of nausea and vomiting with or without diarrhoea has been

recognised in this and other countries during the past twenty years or so. Because of its seasonal prevalence in autumn and winter, it is sometimes called the " winter vomiting disease " and has occurred as outbreaks in maternity units, schools, hospitals, and students' hostels Experimental studies by Jordan *et al.* (1953) suggest that [illegible] The [illegible]

peaks of prevalence

Two *important virus infections, with quite dissimilar epidemio*logical features and seasonal incidence, in which both the respiratory and the anal-oral routes of spread may be important, are poliomyelitis and infective hepatitis.

Surface Infection

The best examples of the spread of surface infections come from wounds of varying degree· the sources and modes of spread tend to be quite different in *small* wounds and *large* wounds. Minor accidental injuries frequently become infected unless treated immediately, and the infecting organism is most often a pyogenic staphylococcus from the patient's own nose or skin (Williams and Miles 1949) Intentional surgical wounds may become infected at the time of operation or during subsequent dressings, and infection is usually spread by contaminated hands and instruments. Devenish and Miles (1939) pointed out that some surgeons could be persistent skin carriers of staphylococci which were " sweated out " and passed [illegible]

risk of aerial spread Even an apparently well-covered wound is not immune to attack, since bacteria may grow through an exudate- [illegible] and particularly blankets which [illegible] portant reservoir for the [illegible]

[illegible]

to infant through the intermediary nurse seems to be the most important means for spreading the germs, although contaminated dust and bedding will, ordinarily, share in the transfer of infection.

Conclusions

From this brief survey, it may be concluded that the paths by [illegible]

broad categories are spread in a community, and of course a particular infection may be spread in a variety of ways Precise knowledge about the mode of spread of the more common infections is still lacking, so that fresh experimental and clinical studies in this field are needed

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THE TRANSMISSION OF VIRUSES FROM ANIMAL TO MAN OTHER THAN BY ARTHROPODS

By

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In so far as the need exists for any infecting virus to reach, in an

two rather obvious but fundamental requirements· one of these is determined by the virus itself—its pathogenic potentiality for man—and the other by circumstances—the opportunity for the agent to encounter its less usual host These two factors are interdependent and difficult to analyse precisely, but in considering some examples of human infection from animal sources, it will be possible to

animals, or domestic vermin, favours transmission Even in such

that many human viruses can be persuaded to infect laboratory animals but only by artificial means such as inoculation into the brain or peritoneal cavity. By the same token, we may suspect that in this sense the potential infectivity of animal viruses for man exceeds the natural limits, to which also a lack of opportunity no

doubt contributes. Any study of the adaptation and evolution of viruses which takes into account these artificial infections will be to some extent incomplete since man is not in the same way an experimental animal.

A large proportion of restrictedly human virus infection is spread from patients or carriers to others by the respiratory route although the illness may not be predominantly one of the respiratory system. Animal viruses, for example those of psittacosis and Q fever, gain access to human tissues in this way and, as will be seen later, the persist

part.

transm

of arthropod vectors is also taken into account. Injection into the tissues by an arthropod provides a particularly good opportunity for a virus to infect a novel host but certain other viruses are specially favoured in this sense so that, although parasites of animals, they may give rise to human infection. Such conditions apply to the transmission of rabies from dogs, wolves, jackals, foxes, vampire bats and other animals and of virus B from monkeys, where the

in this way.

Another example of natural inoculation is found in "cat scratch disease", of which cases were first recorded in France, then in the U.S.A. and recently in Great Britain. The virus aetiology of this condition is strongly suspected but has not been established with

tivity for different animals. Many spread by contagion of the

abraded skin and in this way man is occasionally infected by some of these animal pathogens but from man to man small-pox or variola is transmitted by the respiratory portal of entry. It may be supposed that these viruses have developed from some common ancestor and objective evidence that adaptive changes can occur in them is seen in the vaccinia virus used to immunize against small-pox, this agent is distinct from cow-pox and is thought to have emerged from artificial transfer in animals of variolous material. The ways in which transfer of these agents from one species of animal to another and from animal to man may have brought into existence this large family of viruses is a matter for speculation. There are also interesting but unexplained limitations, where, for example, mouse-pox, a troublesome and not uncommon infection in laboratory colonies, never infects those who handle the diseased animals

species including pigeons, finches, chickens and a number of sea-birds. Pigeons, poultry birds and, in an outbreak in the Faroe Islands, the fulmar petrel have been incriminated as a source of human infection, the causal agent in such instances is referred to by some as ornithosis virus—it differs in certain respects from the virus of psittacine origin and seems to be somewhat less infectious for man. The virus is present in the excreta of infected birds which may appear to be quite healthy but the risk of human infection from, say, a parrot is greater when the bird is ill, then very large amounts of virus dry on the soiled feathers and are later dispersed in the form of dust Although parrots may discharge virus by sneezing and bites from them have been mentioned in reports of

occupied previously by them

Another instance of the importance of virus survival in dust is found in Q fever, a natural rickettsial infection of cows and sheep.

From infected cattle the agent is discharged in the placenta and faeces and the hide is contaminated by excreta from ectoparasites; in contrast with other diseases due to rickettsiae, arthropods do not appear to play a direct part in transmission to man. Those who associate with cattle or handle their carcasses or hides may risk

that inapparent or unrecognized infection may occur in a small proportion of the population, particularly in south-east England

and Stoker, 1950) but the causal virus cannot be said to have got very far as a strictly human pathogen. With animal viruses capable of infecting man such an occurrence is at least a possibility and, indeed, it has been suggested that purely human virus infections may trace

circumstances were such that case to case infection was believed to have been responsible. A similar outbreak in Louisiana (Olson and Larson, 1944) yielded a strain of virus closely resembling that

found to be due to this sheep virus which had been generally regarded as harmless to man This laboratory infection represents transmission at far remove from the natural animal host but emphasizes the fact that only a lack of opportunity for infecting the new species may bar the way to its occurrence In view of the very large amount of virus to be found in the sheep placenta, it may be wondered whether infection has not at times occurred in shepherds and [illegible] laboratory.

The examples given of the different ways by which viruses from animals may endanger human health and life are not only of practical medical importance but, it is hoped, throw some light on the various factors involved in their transmission It would seem that the animals with which man associates for profit or pleasure are rarely at risk on account of human viruses, unlike laboratory animals which have contributed much to our knowledge of them.

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THE TRANSMISSION OF VIRUSES TO VERTEBRATES BY ARTHROPODS

By

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a vertebrate or is found in superficial lesions or excretions may be transmitted by simple *external* contamination of an arthropod vector. Equine infectious anaemia can be spread in this way by stable flies, *Stomoxys calcitrans* (Scott, 1920), and Fenner, Day and Woodroofe (1952) found myxoma virus to be as effectively trans-

Dalmat (1955) have produced evidence which suggests that the

a biological cycle of virus in the mosquito, but the mechanism seems to differ from that of other viruses which have a "biological" arthropod cycle (e g yellow fever), for virus was not found in the thoraces or abdomens but only in the head parts of the mosquitoes used to transmit the fibroma virus, whereas yellow fever virus is found in the salivary glands. Before concluding that a biological cycle of any form exists it will be necessary to exclude the possibility that the mosquitoes act like syringes, in that virus in the infective feed is stored somewhere in the head parts of the vector to be liberated in small quantities with each feed Transmission of myxoma virus (Aragão, 1920, Bull and Mules, 1944, Lockley, 1954, 1955, Ritchie, Hudson and Thompson, 1954, Allan and Shanks, 1955) and of fibroma virus (Kilham and Woke, 1953) by

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Lockley (1954) has noted that corvine birds feed immediately on dead myxomatosis rabbits, and the rabbit flea is occasionally carried by birds (Rothschild quoted by Andrewes, 1954) It is feasible that birds may spread infected fleas long distances (Lockley,

[illegible]

arthropods appear to play the more important role; in some areas lice (*Haematopinus suis*) have been incriminated and elsewhere flying arthropods appear to be responsible (Schwarte and Beister, 1941). The frequency with which mosquitoes become carriers of pox viruses is evidenced by the facility with which Reeves, French, Marks and Kent (1954) isolated no less than seven pox viruses during

[illegible]

cities.

Coxsackie viruses have also been found in house flies and in blow flies, and virus persisted in these species for one or two weeks (Melnick and Penner, 1952). There is no evidence that virus multiplies

in them nor that infected flies play any part in the epidemiology of Coxsackie virus infections (Melnick, Emmons, Coffey and Schoof, 1954).

biological transmission is infected, it continues to be able to transmit virus for the rest of its life, and there is no evidence that infection with an animal virus shortens the life of a mosquito In successful transmission experiments it has been found that during the first few days after an infective feed there is a decrease of virus in the mosquito and that this is followed by an increase in the titre. Although it has been claimed that yellow fever (Whitman, 1937) and West Nile virus (Davies and Yosphe-Purer, 1954), multiply in mosquitoes, other investigators studying the transmission of yellow fever (Davis, Frobisher and Lloyd, 1933) and Eastern (EEE) and

when virus is titrated in species which do not transmit They

deterioration.

From many experimental studies it has been concluded that if successful transmission is to be achieved, the strain of virus used is

of great importance (Davis, Lloyd and Frobisher, 1932; Bates and Roca-García, 1946; Hammon, 1948; Davies and Yoshpe-Purer, 1954). The important factor would appear to be that certain strains give blood titres in the hosts which are too low to infect mosquitoes. In general it may be said that with yellow fever and the equine encephalitides blood titres of 10^{-3} are required to infect 1 to 5 per cent (infection threshold) of susceptible *Aëdes* mosquitoes and infection of 50 per cent of such mosquitoes may be achieved with titres of 10^{-5} to 10^{-6} (Kumm and Laemmert, 1950; Chamberlain *et al.*, 1954). Chamberlain *et al.* have described a method of assessment of vector potential in the arthropod-borne encephalitides, which depends on establishing infection thresholds, infection rates and transmission rates for various species. These data and studies of host preferences, seasonal distribution and relative abundance, etc., permit the deduction of a gradient of potential vectors in any area. The infection threshold appears to be a very important limiting factor Mosquitoes with the lowest thresholds probably find more hosts capable of infecting them and are thus of most importance in the transmission of disease. Congenital transmission of virus infections is not known to occur in mosquitoes (Merrill and Ten Broeck, 1935; Gillett, Ross, Dick, Haddow and Hewitt, 1950; Davies and Yoshpe-Purer, 1954).

EEE virus have been isolated from chicken mites and lice (*Eomenacanthus stramineus* and *Menopon pallidum*) by Howitt, Dodge, Bishop and Gorrie (1948) and also from wild bird mites (*Liponyssus sylvarum*) (Reeves, Hammon, Furman, McClure and Brookman 1947). In spite of numerous attempts only one claim of successful

1948)

While there is adequate evidence that birds play an intermediate part in the transmission of the equine group of encephalitides (Kissling, Chamberlain, Sikes and Eidson, 1954), Murray Valley Fever of Australia (Anderson, 1952) and West Nile virus (Work,

recent virus activity in the area concerned.

The earliest observation on the transmission of a virus disease by ticks appears to be that of Montgomery (1917) who demon-

tionship of louping ill virus, strains of Russian spring summer encephalitis virus and the " Stillerova virus " from Czechoslovakia

Ticks may act not only as vectors but also as permanent reservoirs of virus for in some of the above group, the group, virus is transmitted by all stages of infected ticks and is passed through the eggs

of great importance (Davis, Lloyd and Frobisher, 1932; Bates and

encephalitides blood titres of 10^{-3} are required to infect 1 to 5

hosts capable of infecting them and are thus of most importance in the transmission of disease. Congenital transmission of virus infections is not known to occur in mosquitoes (Merrill and Ten Broeck, 1935, Gillett, Ross, Dick, Haddow and Hewitt, 1950; Davies and Yoshpe-Purer, 1954).

The role which mites play in the transmission of virus diseases is not fully established Congenital transmission of St. Louis encephalitis in chicken mites (*Dermanyssus gallinae*) has been reported by Smith, Blattner, Heys and Miller (1948), and isolations of St. Louis

transmission has been demonstrated. The importance of applying these criteria to the study of virus cycles of transmission involving one or more hosts and one or more vectors will be discussed at the symposium.

with virus. It is also correct from the aspect of *disease* in both mechanical and biological transmission. However, from the point of view of the reservoir of those viruses which are biologically transmitted, the arthropod qualifies better as a host than does the vertebrate

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Colorado tick fever and WEE which can be transmitted by the wood tick (*Dermacentor andersoni*) are similar in this respect. In studying Colorado tick fever virus, Florio, Miller and Mugrage (1950) were able to demonstrate that while the progeny of infected adult ticks showed infection at every stage in their cycle of development, no virus could be recovered from eggs despite the fact that resultant larvae, nymphs and adults which were reared from such eggs were infected. The nature of the non-infective virus in the eggs presents an interesting problem

Before incriminating an arthropod as a vector of any specific disease there are certain essential requirements which must be fulfilled. In the first place the suspected arthropod must be associated in *time* and *place* with the "*person*" of the infected donor and recipient hosts. In the case of biting arthropods this association implies that the suspected vector must bite such hosts. The necessity of applying this criterion may be seen from the following examples *A simpsoni is a monkey to man vector of yellow fever* in some parts of Uganda but in other areas where virus is present in monkeys and *A simpsoni* is also found, there is little human

infections are occurring in the hosts in nature, and the virus must be recovered in the field from the suspected vector. It is usually

(Taylor, 1951).

Even although these criteria are fulfilled it cannot be concluded that *biological* transmission has taken place unless an extrinsic incubation period, viral multiplication in the vector or transovarian

INSECTS AND THE SPREAD OF FUNGAL DISEASE

By

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Since the discovery that fungi cause disease in animals and plants a great number of transmitting agents have been described Among the earliest were the insects noted by Leunis (1847) visiting the

pathologists More recently the part played by insects in other important plant diseases has been elucidated and one animal mycosis is now considered to be predominantly insect-borne.

Insects appear particularly well-suited for the transmission of fungal diseases Many are directly dependent upon living plants and animals for the food and protection necessary for the com-

spores which vary enormously in size, shape and origin The one dominant factor favouring the insect dispersal of a fungus, however, is the possession of "wet" spores which are produced in sticky

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relationship exists in the blossom blight of red clover (*Trifolium pratense*) caused by *Botrytis anthophila* (Silow, 1933), but here the fungus produces its sporing structures on the outside of the anthers. It is curious that both diseases are systemic and seed-borne and that neither has a very marked effect on the vegetative features of the host.

vector. Frazer (1944) has shown how the needle-like shape of the *ascospores of the fungi causing the internal boll disease* (stigmatomycosis) of cotton allows their free passage up and down the stylet canals of the various species of stainer bug vectors, and it seems *probable too that attractive* sugary substances produced with spores, as in the *Sphacelia* state of ergot, for example, have also evolved in conjunction with insect transmission.

Associations between insects and fungi are widespread and numerous Estimates derived from the literature indicate that some 45 different fungal diseases of 34 plant and one animal species (counting *Gramınae* as a single host for ergot) have been claimed to have been transmitted by over 100 species of insects belonging to at least six orders. Sixty-six species of fungi in all classes have been

A classification of insect-transmitted fungal diseases

1. Insect feeding primarily on plant or animal host.
    - (*a*) Transmission of disease without wounding of host· e g anther smut of campions by bees, etc.
    - (*b*) Transmission of disease with wounding of host:
        - (*i*) wounding by transmitting insect; e.g. stigmatomycosis of cotton by stainer bugs.
        - (*ii*) wounding by another agency, e g. epizootic lymphangitis by pasture flies; oak wilt by beetles, etc.
2. Insect feeding primarily on fungus or its metabolic products
    - (*a*) direct transmission, e g. ergot, by flies feeding on honeydew.
    - (*b*) indirect transmission, e g. diploidization of rust mycelia by flies.

The simplest type of transmission by insects occurs during the pollination of flowering plants. In anther smut of campions

[illegible]

extent, a symbiotic one for the fungus cannot infect without previous aphid damage and the aphid is protected, even overwintering in the crevices of the cankers

Those insects attracted to plant pathogenic fungi as a source of food are chiefly Diptera (especially *Mycetophilidae* and *Muscidae*) and Coleoptera and the inoculum carried by them is picked up [illegible]

beings. The imperfect or *Sphacelia* state of the ergot fungus (*Claviceps purpurea*) is produced on the outside of affected grass or cereal flowers and the conidia remain in an exuded drop of sweet, sticky secretion known as "honey-dew" Stager lists 37 species of flies and beetles which he observed visiting these secretions (see Atanasoff, 1920). Visits to uninfected flowers result in the transfer of the spores to a receptive surface on which germination and [illegible]

fungus *Puccinia suaveolens* Later Râthay (1882) linked this property with the attraction of insects to the spermagonia or, as they are now called, the pycnia, of rusts He recorded 139 species of insects visiting these organs on a variety of plants and, as Plowright (1889) retells, he "noticed some flies fly away from the leaves (of *Euphorbia amygdaloides* affected with *Endophyllum euphorbiae-silvaticae*) and alight on a window pane Closer scrutiny showed that the flies had left their wet footmarks upon the glass These footmarks were found to contain the spermatia (pycniospores) of *Endophyllum*."

[illegible]

to the plant breeder, who is constantly having to produce new varieties of cereals resistant to particular races of rust and each time a new virulent race arises a new breeding programme to combat it must be instituted. In recent years the United States has been swept by a new race of stem rust of wheat (*Puccinia graminis tritici*), Race

respectively. The spores and hyphae of the fungus (*Leptosphaeria*
of the body of

a rather more
ith the basidio-

inoculated with oidia and hyphal fragments, so that the inoculum is placed well into the wood of the tree. The exact role of the fungus in the nutrition of the larva has not been fully determined but it seems likely that the hyphae form the major part of the larval food and moreover, as Parkin (1942) has shown, the larvae themselves

attracted by the characteristic odour produced. Subsequently these insects, by crawling over the surface of fresh wounds, inoculate healthy trees and complete the cycle of infection (Fowler, 1953; Stessel and Zuckerman, 1953)

In the category of insect transmission following wounding by another insect comes the only example of an insect-transmitted animal mycosis. Epizootic lymphangitis of horses and mules is caused by the dimorphic fungus *Histoplasma farciminosum* and it was generally assumed that infection was either passed from one
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own)
which visit the ulcerated cutaneous lesions. Healthy animals are
upon the blood and lymph oozing from

insect-borne

Apple canker affords a further example of infection following

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15B, to which almost every known variety of wheat is susceptible (Stakman, 1955) The race was first observed on and around barberry bushes (*Berberis* spp) which are the secondary (aecial) host of *P. graminis* and it seems probable that the dicaryosis giving rise to the new race was effected through the transmission of the pycniospores by insects.

From this outline of the different methods by which insects

the disease and classic among such cases has been that of chestnut blight in North America. Following its presumed introduction on imported Japanese trees, the fungus (*Endothia parasitica*) virtually wiped out the native chestnut in less than 25 years, having been

must be borne in mind that it is only the one relationship between

of value in the control of insect-borne diseases Co-operation between mycologists and entomologists is thus becoming increasingly necessary and the spread of Dutch elm disease, chestnut blight and oak wilt should provide sufficient incentive for further investigation.

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droctonus) and blue stains.

THE TRANSMISSION OF PLANT PATHOGENS BY SEED

By

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ALL kinds of plant pathogens are known to be transmitted by seed—viruses, fungi, nematodes, bacteria and insects—and there is scarcely a more effective method of distributing pathogens within a crop or from country to country than by seed I do not propose to

Effect of the pathogen on the seed

In some cases the relationship between pathogen and host is loose and transmission seems almost to be fortuitous, or the con-

but I propose to take a few examples which are more or less clear cut to illustrate these points

Pathogens which do not injure the seed by which they are transmitted

Mycosphaerella pinodes may pass down the funicle from the pod and become established in the seed without any appreciable or visible damage. When the seed germinates, however, the fungus becomes active and attacks the seedling, causing greater or less

and spots on the seed as indicating the presence of the fungus *Ascochyta imperfecta*. This fungus also occurs on clover in America where, however, the same symptoms can be caused by a severe disease called "black patch" not yet recorded in Britain This latter fungal disease is only known to be transmitted by seed and has no known spore form, so that it is classed in *Mycelia sterilia* The two infections can be distinguished in the laboratory by incubating the seeds on water agar, when the types of growth produced are quite distinct.

The control of this whole group of diseases is extremely difficult because of the varying degrees of damage to the seeds caused by the pathogens and the danger of damaging the seed while attempting to control the pathogens.

Pathogens which kill the seed transmitting them

An excellent example of this group is provided by the fungal disease of rye-grass called blind seed disease. In this disease the

of the ryegrass and the young ovaries are infected by air-borne ascospores which germinate to form a second, asexual form of spores which are distributed in water While these spores are forming on the testa of the developing seed, mycelium is permeating the seed, where it becomes established Infected seed when sown

spores but in this case the spores germinate as soon as they are disseminated and the fungus enters within the seed Control of this disease is extremely difficult owing to the fungus being so deep-seated, but recent interesting work in Canada and America has shown that antibiotic substances on the seed inhibitory to the fungus can be artificially increased in potency so that infection can be killed without the use of chemicals.

Many of the virus diseases transmitted by seed also fall into this category in that transmission occurs without injury, but the relationship to the seed is very much closer, as for instance in mosaic of lettuce, and disinfection virtually impossible. From 1956 it will be necessary for lettuce seed entering this country to be free from lettuce mosaic The sclerotia of fungi and galls of nematodes are transmitted as macroscopic contaminants of seed samples which often resemble seed. If the size and shape of these structures are fairly constant and distinct from those of the seed then they can be [illegible]

[illegible]

cleaned samples of wheat, are now rarely found. On the other hand [illegible]

[illegible]

later effect another crop such as artichokes or carrots. In such cases it is rarely demonstrable that infection was in fact seed-transmitted. The disease clover sickness already mentioned involves the fungus *Sclerotinia trifoliorum* and the nematode *Ditylenchus dipsaci* which [illegible]

[illegible]

Pathogens which injure to a greater or less degree the seed transmitting them

This is a group of very great importance in plant pathology and [illegible]

[illegible]

sign of infection on the seed. For instance, in peas the fungus

Oregon from feeding chewings fescue cleanings that contained nematode galls When heavily infested screenings of chewings fescue were fed to sheep and rats in controlled experiments at the Oregon Agricultural Experiment Station, the animals were killed. Nervous phenomena in sheep and gangrenous development in rats, similar to ergotism, also appeared. The poisonous principle is not known."

Another example of the connection between animal pathology and plant pathology involving seeds which may be used to illustrate this point does not involve infection by a pathogen but a condition of mineral deficiency Manganese deficiency in the oat crop causes a disease in the field known as grey speck and the seed from such a crop although apparently normal contains a greatly reduced proportion of manganese. Seeds from healthy oats contain approximately 40 or 50 parts per million but that from a crop affected by grey speck has only about 20 parts million. If such grain is used for feeding poultry without a supplementary source of manganese the flock may develop symptoms such as cannibalism, perosis and bad hatching of eggs

I would like to suggest that there is here a field of work which should be much more fully explored, both in this country and abroad, than is at present the case The study of seed pathology in itself involves many different aspects of biology and as a mycologist I welcome this opportunity of recording my gratitude to my colleagues specializing in bacteriology, nematology, entomology and many

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their formation. Further if the seed is kept in store for two years the fungus dies with the infected seed and the remaining healthy seed can be sown safely The blind seed fungus was present in this country for at least 50 years before it was found in 1940, following its discovery in New Zealand although it was known to occur on rye in France at the end of the nineteenth century.

Transmission of one pathogen by another

I have already suggested that infection by several pathogens can occur in close association and this may be illustrated by the pathogens which occur in the grass "chewings" fescue, *Festuca rubra* var. *fallax*. Seed of this species is imported from New Zealand and is

bacterial disease of fescue is recorded from the field but a seed-

of the nematode *Anguina tritici* but can only attack the plant in the presence of the nematode, without the nematode, it is innocuous.

Seed-borne pathogens and animal poisoning

This problem first came to the notice of my colleagues and myself when working with the blind seed disease of ryegrass and we found that it had been discovered in France in 1890 because bread

there is ye
involved
fungi may

itself contains a toxin

The nematode disease of chewings fescue mentioned as being

THE TRANSMISSION OF PLANT VIRUSES BY INSECTS

By

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My subject is already embarrassingly large, but as no one else at this meeting is dealing with other ways by which plant viruses are transmitted, I think I must extend it still further, at least to the [illegible]

insects almost certainly do more transmitting than all other animals put together.

Vectors of plant viruses have been identified in most of the different types of insect that feed on plants, but by far the most have been in those that feed by sucking juice, chiefly aphids and [illegible]

largely untested, for entomologists have been reluctant to seek vectors among biting insects, almost unreasonably so considering the early success in transmitting one or two viruses with beetles and grasshoppers. This phase of almost exclusive attention to aphids and leafhoppers is now passing, and as a result a rich crop of new [illegible]

damages plants excessively, but it is a crude, haphazard method of [illegible]

transmitted much more readily by aphids that have fasted for some time before feeding on an infected plant than by those that have been feeding continuously. The fasted aphids transmit more often only if they feed for short times on the infected plants, and they become increasingly less likely to transmit the longer they remain [illegible] para- [illegible] fed [illegible] the more likely they would be to transmit. The phenomenon has no certain explanation, but it seems probable that this type of virus occurs predominantly in the epidermal cells of infected plants and that fasted aphids are more likely than those that have recently been feeding to imbibe sap when their stylets penetrate the epidermis. As the vectors' feeding time on the infected plant is prolonged, their [illegible] to act as a vector may depend on whether or not its stylets are so constituted that they can absorb and retain the particles of the virus Of two species that can transmit a virus, one often does so more readily than the other Such differences may reflect either the relative abilities of their stylets to retain the virus, or the relative extents to which the two species imbibe juice from epidermal cells of infected plants.

Not all viruses whose vectors soon cease to be infective can be acquired from infected plants during feeding periods of a minute or less The vectors of some strawberry viruses and of a lettuce virus can transmit only for an hour or so after leaving an infected plant, but they need to feed for at least an hour on such a plant to become infective, and the longer the vectors feed there, the more likely they are to transmit. These viruses are ones that have either not been transmitted by manual inoculation with plant sap, or transmitted so only with difficulty. They probably occur at much lower concentrations than those we have already discussed, and they may be differently distributed in leaf tissues, possibly being predominantly in other cells than the epidermis.

The opposite extreme of behaviour is shown by some aphid-transmitted viruses, and probably with all those transmitted by leafhoppers, white-fly and thrips. Characteristically their vectors,

described as vectors is no reason to attribute specificity to grasshoppers, for many others could probably sometimes do the same thing, by getting their mouths contaminated with virus while feeding on an infected plant before feeding on a healthy plant. Indeed, these two viruses are so easily transmitted by mechanical inoculation with plant sap that the most puzzling thing about them is to understand why they are not also regularly transmitted by

feeding were found to transmit, and these retained their ability to infect healthy plants for some days after they had ceased to feed on infected ones.

Specificity of transmission becomes much more evident immediately we start to consider the transmission of viruses by sucking vectors. First, there is what can be called group specificity, summarized by the general statement that no virus that has been experimentally transmitted by individuals of one insect group, say the aphids, has also been transmitted by individuals of other groups, such as the leafhoppers, white-flies, mealy-bugs or thrips. Secondly,

extremes as examples. The main differ-

vector, for when one virus has several vectors they all behave in very much the same manner, whereas the same species of insect may show different types of behaviour when transmitting different viruses

[illegible] infective vectors are born virus-free and acquire viruses only by feeding on infected plants.

Several leafhopper-transmitted viruses have been proved to multiply in their insect vectors Unequivocal evidence was first provided by experiments showing that the offspring of insects carrying clover club-leaf virus continued to be infective over more than 20 generations while denied the opportunity to feed on infected plants Subsequently, following the discovery that the aster leafhopper became infective when inoculated with extracts from leafhoppers carrying aster yellows virus, this virus also was shown to multiply in its vector, for it maintained itself indefinitely when insects were inoculated in series. Proof of multiplication has yet to be obtained with any virus transmitted by insects other than leafhoppers, but it is reasonable to assume that viruses with pro- [illegible]

those taxonomists who wish to use animal and plant hosts as their first criterion for deriving a classification The opinion is widely held that severe disease is characteristic of a recent association between host and parasite and that long association leads to decreased virulence. If there is anything to this opinion, then these viruses should perhaps be regarded as primarily insect viruses, for they cause severe diseases in some of their plant hosts but seem to be as harmless to their insect vectors as are other plant viruses that do not multiply in the insects that transmit them.

An understanding of the way in which an insect behaves as a vector has more than academic value, for the type of behaviour is important in determining the extent to which a virus spreads in crops. Spread is not something that can be computed solely from the number of initial sources of virus and of potential vectors. It will be determined by the way in which the feeding behaviour of the vectors affects the likelihood they will be infective when they move, and on the frequency with which they move. Of two species that seem equally good vectors in experiments, one may be the predominant vector in field crops, even though the other may occur in greater numbers, simply because the one moves much more often. The great restlessness of *Myzus persicae* probably accounts for its prime importance as a vector of many virus diseases of our crops, although it is rarely as numerous as other species that can transmit Similarly, although wingless aphids can transmit and occur much

having once become infective, remain so for long periods, often for the rest of their lives. There are a few exceptions, but typically these viruses are not transmitted to healthy plants by manual inoculation with sap from infected ones; some of the viruses, however, can be successfully inoculated to their leafhopper vectors by injecting them with sap from infected plants or with blood from other infective insects. There is evidence that at least some of these viruses infect healthy plants only if they are introduced into the phloem and that they also occur predominantly in the phloem of infected plants.

Within the large group of viruses whose vectors remain infective for long periods, individuals behave in a variety of ways. Some viruses can be acquired by their vectors while feeding on an infected plant for periods of only 10–15 minutes, whereas vectors of others may need to feed for hours The minimum time is probably set by the length of time taken by the insects' stylets to penetrate to the phloem, and the differences in the average acquisition time with different viruses may reflect their relative concentrations in the phloem of infected plants These viruses cannot be transmitted to healthy plants immediately vectors have acquired them by feeding on infected ones, but the "latent" period between the two events varies from an hour or less with some viruses up to many days with others Transmission of all of them seems to require that the [illegible]

depend on the permeability of its gut to the virus. The vector of maize streak, *Cicadulina mbila*, exists in two forms, only one of which can normally transmit. Crosses between the two forms show that the ability is determined by a dominant gene, but indi- [illegible]

on an infected plant to circulate through the body of the insects and be ejected with the saliva. Experiments with some such viruses have shown that the time for which vectors remain infective depends on the length of time they fed on infected plants, those given short infection feedings soon ceasing to be infective. It seems, then, that vectors of these viruses contain only that quantity of virus they imbibe from infected plants. The position is quite different with viruses that have latent periods in their vectors of several days. Provided only that their vectors feed long enough to acquire virus, extending the length of time they spend on infected plants does not increase the length of time for which they remain infective, once

Day, M F and Bennetts, Margaret J 1954 *A review of problems of specificity* [illegible]

[illegible]

viruses by aphides, a comparative study of a non-persistent and a persistent virus having host plants and vectors in common" *Proc Roy Soc. B*, **133**, 200–19

more abundantly than winged ones, most never transmit even if they become infective, for they do not move; transmission is mainly the prerogative of the minority that fly. Also, the fact that leafhopper-transmitted viruses often reach a prevalence rare with aphid-transmitted ones in part *reflects the greater mobility of leafhoppers.* There are, though, other reasons, for leafhoppers usually remain infective for long periods, whereas with most viruses aphids soon cease to be infective.

A knowledge of the behaviour of a vector in transmitting a virus is particularly important now, a time when many new insecticides

the incidence of an insect-transmitted disease can increase in a crop: one, by spread from plants already infected in the crop, and, two, by insects that are carrying viruses when they come into the crop. Some of the persistent insecticides kill aphids within a few hours, and they are abundantly adequate to prevent infestations from developing in the crop. By doing this they can be expected to *decrease the incidence of aphid-transmitted viruses, but the extent* to which they do so will differ with different viruses, and this has been the experience in practice. They have the greatest success in preventing spread from infected to healthy plants within a crop, especially when the virus is one whose vector does not become able to transmit immediately it has fed for a short time on an infected plant. They have least success in preventing infections caused by aphids that are already infective when they come into a crop, although with vectors that remain infective for long periods, and

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THE TRANSMISSION OF TRYPANOSOMES AND ITS EVOLUTIONARY SIGNIFICANCE

By

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TRYPANOSOMES belong to the flagellate family Trypanosomidae, which has been studied perhaps more fully than any other groups of protozoa, on account of the practical and theoretical interest attached to these parasites, whose economic importance is due to the fact that members of two of its genera, *Trypanosoma* and *Leishmania*, are responsible for a number of diseases in man and domestic animals.

The transmission of trypanosomes, which is the subject of this

to the vertebrate host again

Transmission of insect flagellates

As an example of flagellates restricted to an invertebrate host we may take *Herpetomonas* occurring in fruit-flies, *Drosophila*. After multiplying in the mid-gut in the flagellate stage, the parasites pass into the hind-gut, where they eventually lose their flagellum and

contaminative method of transmission Trypanosomid flagellates transmitted in this manner are found in diverse insects, both blood-sucking and non-blood-sucking.

(b) Inoculative method

We now turn to a group of trypanosomes in which the life cycle follows quite a different pattern. They comprise a number of species of medical and veterinary importance, all of which occur in Africa and are transmitted by tsetse-flies (*Glossina*) As examples we may take *T. gambiense* and *T rhodesiense*, which cause two types [illegible]

into the proboscis and thence—*via* the hypopharynx—into the salivary glands, where the infective metacyclic trypanosomes are produced in about 2–4 weeks

[illegible]

inoculative method of transmission.

Transmission by this method also occurs in some other tsetse-borne trypanosomes pathogenic to cattle, e g *T vivax* and *T congolense*, but in these species the infective forms do not invade the salivary glands but are restricted to the proboscis of the vector

(c) Mechanical method

In the types of transmission considered above, the flagellates *must complete their life cycle in the intermediate host before they* become infective to the vertebrate host In addition to this *cyclical* transmission, some trypanosomes may be transmitted *mechanically* both by their proper vectors and by other blood-sucking insects. In this case the blood trypanosomes taken up by the insect merely survive in its proboscis, without undergoing any development, and [illegible]

flies (Tabanidae).

Transmission of trypanosomes

We can now consider the development and transmission of trypanosomes All members of the genus *Trypanosoma* live in the blood of vertebrate animals, some—like the trypanosomes of rats, sheep, and cattle in this country—being harmless to their hosts, while others are path[illegible] of man and domestic mammals [illegible] infected blood of a [illegible] multiply in the alim[illegible] transformed into stages corresponding to those found in *Herpetomonas*, but eventually these flagellates give rise again to a special *type of trypanosomes, known as metacyclic forms, which constitute* the infective stage It is important to note that, until this stage of [illegible] of transmission to the vertebrate.

(a) Contaminative method

[illegible] type of transmission we may [illegible] develop in the mid-gu[illegible] the infective metacycl[illegible] weeks. Transmission [illegible] membrane [illegible] transferred [illegible] infective stages are represented by unprotected flagellates.

medium and is peculiar to the pathogenic trypanosomes of mammals, is not so clear, since no comparable life cycle is known among purely insect-flagellates. However, it is conceivable that this life cycle is a secondary acquisition in certain trypanosomes which originally developed in the hind-gut of their insect-vectors. It is possible that such trypanosomes were taken up by tsetse-flies, which began to transmit them mechanically to new mammalian hosts, but in the course of time—when the trypanosomes adapted themselves to cyclical development in the proboscis and/or salivary glands—tsetse-flies became their new intermediate hosts

In *T. vivax* we have an example of the initial phase of this adaptation, when the development does not go beyond the mouthparts

While in the case of *T. cruzi* practically 100 per cent of the bugs fed on an infected mammal become infected, the infectivity of tsetse-

readily revert to mechanical transmission. Examples of this transformation are provided by *T vivax*, which has established itself

transmission by direct contact from mammal to mammal.

Conclusion

In concluding this review it must be admitted that—like all hypotheses—the views advanced regarding the phylogeny of trypanosomes contain an element of speculation. Nevertheless, the regular

Effectiveness of transmission

If the different methods of transmission are compared, it will be seen that their effectiveness—assessed by the degree to which they ensure infection of new hosts—improves progressively as we proceed from the insect-flagellates to mammalian trypanosomes. Thus, in the case of *Herpetomonas* enormous numbers of infective leishmanial forms escape from the hind-gut with the droppings, but only some of them are accidentally eaten by and infect new insect-hosts. In the case of direct contaminative transmission there is, therefore, a considerable element of chance, since the majority of the parasites perish without finding a new host. However, in the case of *Trypanosoma cruzi* the vector deposits the infective forms directly upon vulnerable parts of the human body, thereby considerably increasing the chances of successful infection. A further progress in transmissibility is found among the tsetse-borne pathogenic trypanosomes (*Brucei*-group, etc.) Here nothing is left to chance, for the infective forms are injected directly into the mammalian body through the bite of the insect.

Evolution of trypanosomes

Having described the main patterns of life history and transmission in trypanosomes, we are in a position to compare them and make certain deductions. It has already been mentioned that the

into their life cycle an alternation between invertebrate and verte-

ages of develop-

an therefore be

Herpetomonad

biogenetic law

among the protozoa.

evolution through which it has passed.

CYCLICAL TRANSMISSION OF HAEMOSPORIDIA

By

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THE title of this paper refers to the Haemosporidiidea, a sub-order in which are included the Plasmodiidae, the Haemoproteidae and by some workers the Piroplasmidae In a short paper it is probably more interesting to restrict the scope of the subject than to try to include everything, so the piroplasms are omitted and the paper will chiefly relate to the malaria parasites of the genus *Plasmodium*. The [illegible] repeat here, and it is accordingly proposed to discuss the subject from two angles (1) abnormal methods of transmission (non-arthropod, but involving the asexual cycle and therefore " cyclical ") and (2) factors influencing transmission by the mosquito

Abnormal methods of transmission of malaria

Two interesting forms of malaria transmission are known, congenital malaria and transfusion malaria

Congenital malaria

Few protozoal diseases are transmitted congenitally, but malaria occasionally behaves in this way, probably when the infection is [illegible]

Transfusion malaria

To-day, transmission of malaria in the course of blood transfusion is not uncommon, though in temperate climates it is fairly easy to prevent potential malaria carriers from acting as blood donors. The problem is more difficult in countries like India where it is

such drugs *in vitro* might be ineffective. Thus cases of malaria

gametocytes and immediate tertian periodicity are less reliable guides to the origin of the infection.

Factors concerned in mosquito transmission of malaria

caught *Anopheles gambiae* (4–15 per cent or more) do not indicate that this species is actually a better host than, say, *A. culicifacies* which normally does not show a rate higher than 0 01 per cent in nature. In the laboratory both these species can be easily infected

parasite in the laboratory Thus Young and Burgess (1948) found

squitoes to *P. vivax* was as

ennis 86, *A quadrimaculatus*

and *A. albimanus* 2. And

But each species of mosquito is not genetically uniform, and Huff (1929) showed that it was possible to breed a line of *Culex pipiens* which after a few generations of selection was able to act

as host in 91 per cent of cases to *P. cathemerium*, while another line bred for insusceptibility was reduced to infection rates of the order of 7 per cent.

It is interesting to note that as an malaria has a wide range of mosquito hosts– of mosquitoes: *Anopheles* and much more hos species. *P. berghei* is perhaps the most restricted in its range; high rates are found in nature in *A. dureni*, but the most extensive trials in laboratories all over the world have hitherto failed to produce a good laboratory vector. *P. malariae* is an equally difficult species to work with, but this time it is probably because it is such a poor gametocyte producer, several species of *Anopheles* are susceptible

easily; on the contrary, a European strain of *P falciparum* gave a 93 per cent infection rate in the indigenous *A maculipennis atroparvus* (Shortt *et al*, 1951) But this indigenous factor does not often play a part, because mosquitoes entirely unrelated geographically to the parasite often prove to be extremely efficient vectors, e g *P. cynomolgi* of the East Indies grows easily in *A maculipennis* of Europe, *P. ovale* of the Philippines in *A quadrimaculatus* of the U.S.A.

What is the factor influencing susceptibility of the mosquito?

various mosquitoes including the indigenous *A. gambiae*. Large

zoites developed in the oöcysts, but when rupture occurred, the sporozoites were immediately exposed to some lethal influence; even suspensions of 13 mid-guts containing many ripe oöcysts were unable to infect new monkeys. A few sporozoites reached the salivary glands, but were degenerate or dead and in every case proved non-infective to monkeys After a few days, none could be found at all in the salivary glands. Sections of the abdomen were made at the time of rupture of the oocysts to study what had happened to the sporozoites, but nothing significant was found—neither a tissue reaction around the ruptured oocysts, nor phagocytosis of sporozoites, and it is assumed that the latter are lysed by the body fluids of the insect

Recent work by Weathersby (1952) has considerably advanced our knowledge of this subject. He demonstrated that the full cycle of sporogony could be completed after the introduction of

ways

1. No oökinete formation (*H. kochi* in *Mansonioides africanus*, etc)
2. Failure of ookinete to penetrate wall of mid-gut (African *P. falciparum* in European *A maculipennis*).
3. Poor or abnormal growth of oocysts (*P berghei* in *Anopheles stephensi*, etc)
4 Lysis of sporozoites (*P. gonderi* in *A. maculipennis*)

It seems unlikely that any of these adverse factors could be circumvented by experimental means, except perhaps in the case ... might be due to lack

[illegible]

not in the case of the other three factors, where lack of understanding between host and parasite is probably as great as between man and piroplasms, or cattle and the virus of yellow fever.

Transmission of haemoproteids

The transmission of *Leucocytozoon* shows features of great interest, because apparently there is an essential difference here from all other genera of the sub-order The invertebrate host is *Simulium*, at least in North America, and in places where this insect is absent—like Egypt—the parasite also does not occur. Unfortunately, *Simulium* is one of the most difficult insects to use in experimental work, because it is practically impossible (*a*) to colonize it and (*b*) to make specimens reared from pupae, feed. [illegible]

maturity in *Culex tarsalis* in 4 days, but the details of development were not observed.

[illegible]

Haemoproteus, which develops in various genera of hippoboscid flies Until last year, development was thought to be confined to *Pseudolynchia*, but in 1954 Baker showed that *Ornithomyia* was the vector in England.

Another pupiparous fly (a nycteribiid) was shown by Mer and Goldblum (1947) to transmit the malaria parasite (*Polychromophilus*) of insectivorous bats in Israel This group of flies is confined to bats and we must look elsewhere for the unknown vector of similar parasites in monkeys, lemurs, squirrels, elephant shrews, sitatunga, etc.

In conclusion, I have said nothing about the actual mechanism of transmission, i e. how the parasite is transferred from the invertebrate to the vertebrate host. This process is normally confined to the passage of sporozoites, in the saliva, during biting It is possible, however, that, in certain cases, the animal becomes infected from swallowing the arthropod, which is known to happen when birds eat *Ornithomyia* containing trypanosomes and subsequently develop the infection.

Perhaps the most mysterious circumstance of transmission of the Haemosporidiidea is the change of environment experienced by the

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THE TRANSMISSION OF SCHISTOSOM

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S. haematobium in Egypt. Human schistosomiasis is n
to be endemic in many tropical and sub-tropical cour
India as a notable exception, and it has been estimated tl
some 200 million people may be infected

The three chief schistosome species, *S. japonicum*, *S. m*
S. haematobium have identical life histories except that the
vectors are distinct and that the site of the mature wo
body of the definitive host is largely different *S. japo*
S. mansoni occupy the mesenteric veins whilst *S haem*
found to the greatest extent in the vesical plexus

metre in length and the females rather longer. The r
body of the adult male possesses a gynaecophoric cana
tudinal groove in the ventral surface—which, in the r
carries the longer and much narrower female, whose a
posterior ends usually project beyond those of the male.

slightly behind the ventral sucker. It has been general

that for purposes of egg-laying the fertilized female leaves the male, moves anteriorly, deposits her eggs in the narrower venules and retreats once more to the male There is considerable doubt that this is the case. In the author's experience of many thousands of autopsies of infected experimental animals, no instance has ever been observed of a female separate from, yet anterior to, the male and it seems much more likely that the female reaches forward from her position in the gynaecophoric canal, deposits her eggs in the narrowest venule available and retracts for further fertilization. Each egg is equipped with a spine, either lateral as in *S. japonicum* and *S. mansoni*, or terminal as in *S. haematobium*, the function of which appears to be to assist in retaining the position of the egg in the venule. Failure of the female to reach venules sufficiently narrow to accomplish egg-retention may well account for the large numbers of eggs that are washed back with the blood flow and deposited in the liver and other tissues Successfully deposited eggs work their

faeces or urine Those eggs washed back to the liver continue to develop, but eventually become encapsulated by liver or other

at the terebratorium and the other at the antero-lateral margins of the body.

loses its cilia and is converted into a primary sporocyst The primary sporocyst migrates through the body tissues of the snail in the direction of the hepato-pancreas and ovotestis At about the 15th day it becomes a secondary sporocyst—a convoluted organism [illegible]

The cercariae migrate through the tissues of the snail and emerge at the region of the mantle collar From 3–5 weeks after infection cercariae are discharged daily, either until the death of the snail or until the infection is spontaneously eliminated The sex of the schistosome is determined at the time of fertilization of the ovum, but there is no sexual dimorphism in the miracidial or cercarial [illegible]

[illegible]

vertically upwards to the surface film and then sink, motionless, vertically downwards This vertical alternation contrasts with the movement of *S japonicum* cercariae which tend to accumulate at the surface film, where they lie horizontally beneath it. According to species, the cercaria possesses 5–6 pairs of penetration glands, the function of which is to assist in penetration of the skin of the definitive host

Following adherence to the skin by means of the oral and ventral suckers, cercarial penetration is effected by a combination of [illegible] and extension and [illegible] on is rapid, some [illegible] n in experimental [illegible]

[illegible]

heart. From there, they arrive in the lungs a few days after initial penetration. The route from the lungs is not known with certainty. Some workers contend that the schistosomulae cross the pleural cavity, penetrate the diaphragm and then enter the liver; others maintain that they return to the heart by way of the pulmonary veins and are distributed in the aortic circulation, eventually arriving in the liver by way of the mesenteric arteries and veins Here, much remains to be found out but, at all events, from experimental evidence, they reach the liver 2 to 3 weeks after penetration of the skin. Here they develop, reaching sexual maturity at 28–42 days from infection, if both sexes are present. Pairing of males and females commences at this time and is followed by migration of the pair from the liver to the mesenteric or vesical veins, where they develop to complete maturity. Egg-laying commences and the cycle is complete, the eggs appearing in the excreta 8–10 weeks after cercarial penetration. From experimental evidence, it appears that when unisexual infection of the definitive host occurs, male worms develop normally

[illegible]

of the schistosomes from the liver to the egg-laying site follows attainment of maturity by the females.

In spite of its complexity, the success of the schistosome life cycle is undoubted. The association of a sexual phase in the definitive host with an asexual phase in the molluscan host offers

[illegible]

during one day, reaches astronomical proportions. Certainly,

in an endemic area offers additional opportunity for dissemination of the species With *S mansoni* and *S. haematobium* no important animal reservoirs are known.

Human infection results from contact with water containing [illegible] ion of the indigenous [illegible] pursuits or domestic [illegible] The relatively unim- [illegible] communities arises [illegible]

account for high incidence. In other countries, especially in the Far East, the use of human excreta in agriculture plays a large part in promoting schistosomiasis. The presence of the snail vectors is an obvious necessity before schistosomiasis can occur and many factors such as depth and speed of water, seasonal variation in temperature, organic and mineral content of the water, play their part in determining the distribution and abundance of snails. The requisite temperature for sporocyst development within the snail, coinciding with the range of temperature tolerated by a potential snail vector, probably contributes greatly to the incidence of snail infection in any given locality. So, it may well be that snails not yet found infected in the field are susceptible to infection under laboratory conditions but, in virtue of their normal ecological environment, are unlikely to prove vectors The study of the ecological requirements of the vectors is very much in its infancy [illegible]

guided agricultural practices.

[illegible]

unresolved. It has been stated that labour continuously employed in infected water acquires immunity to infection. Again, in areas where transmission is more seasonal, annual infection followed by treatment is not uncommon In schistosome dermatitis, caused by cercariae of non-human origin, repeated exposures lead to great [illegible]

seasonal, the carry-over of dermal sensitization would not be adequate to resist subsequent cercarial invasions. Until adequate therapeusis is available human experimentation in this problem is undesirable.

The resistance to reinfection of the molluscan vector is not known.

[illegible]

impossible. This factor must play an important part in the maintenance of the vector strain because infected snails are almost invariably sterile and wholesale infection would lead to elimination of a snail community. So, as long as the mature snails are immune to infection—whatever the cause may be—a plentiful supply of young is assured and both molluscan host and parasite may flourish. So, it may not be possible to determine the susceptibility of the molluscan vector to reinfection because, by the time spontaneous elimination of the original infection occurs, age resistance would [illegible] the fecundity of the snail vector is such that

[illegible]

[illegible] of experience cannot hope to cope with the

[illegible]

tropical countries, schistosomiasis probably ranks in importance second only to malaria, yet the relative emphasis placed on the study of the respective vectors is completely disproportionate to the need. There is opportunity and necessity to encourage and stimulate research in malacology.

THE TRANSMISSION OF EXPERIMENTAL FILARIASIS

By

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adult worms live in particular tissues and parts of the human host and the microfilariae which they produce pass into the blood-

are to be found in standard works on tropical medicine or medical entomology and current literature continues to supplement our knowledge in important ways It is not my purpose to deal with these human infections much beyond this brief indication of the range of biological material concerned

1. Filariasis in animals and birds

Most of our knowledge of the biology of filarioid infections has been based on researches in the field or in the laboratory with the human infections, although it would be wrong to omit to mention the contributions of mosquito-borne filariasis of dogs, recent work

seasonal, the carry-over of dermal sensitization would not be adequate to resist subsequent cercarial invasions. Until adequate therapeusis is available human experimentation in this problem is undesirable.

The resistance to reinfection of the molluscan vector is not known. Age resistance, in certain species at least, plays an important part. Generally, young snails are more susceptible to infection and resistance increases as the snails grow older, until infection becomes impossible. This factor must play an important part in the maintenance of the vector strain because infected snails are almost invariably sterile and wholesale infection would lead to elimination of a snail community. So, as long as the mature snails are immune to infection—whatever the cause may be—a plentiful supply of young is assured and both molluscan host and parasite may flourish. So, it may not be possible to determine the susceptibility of the molluscan vector to reinfection because, by the time spontaneous elimination of the original infection occurs, age resistance would interfere. In any event, the fecundity of the snail vector is such that reinfection of the host would be of little epidemiological importance.

The outstanding gap in our knowledge of the transmission of schistosomiasis centres around the lack of information concerning the ecology and taxonomy of the molluscan vectors. Up to the [illegible]

the taxonomy of the group and the ecological relationships of its members is essential to any logical approach to control of the disease. As a public health problem in many tropical and subtropical countries, schistosomiasis probably ranks in importance second only to malaria, yet the relative emphasis placed on the study of the respective vectors is completely disproportionate to the need. There is opportunity and necessity to encourage and stimulate research in malacology.

1951; Williams, 1948) These characteristics of size and accessibility seemed favourable to numerical studies of the parasite at different stages of its life cycle.

3. Quantitative Transmissions

An important, if not the most important, aspect of the biology of a parasite dependent for its survival on arthropod-transmission is the reliability of its transmission. Quantitative aspects of this important event were tackled in two ways. In one (Scott, 1947;

example, in one particularly well-studied series of mites (Freer, 1953) infected from a cotton-rat with 348 microfilariae per cu mm of peripheral blood the range of uptake was from 21 to 695 microfilariae with a mean of 199 per mite But no mite developed more than 42 infective larvae.

leakage from lacerated capillaries and into which microfilariae tend to escape less easily than the blood. The peculiar habit of the mites

continuous strain for experimental work in the laboratory. This was commonly because the vector was not known. Filarioid worms, unlike protozoa, spirochaetes and other comparatively simple pathogens, are not suited to continuous maintenance as a laboratory strain by *in vitro* culture, simple passage methods, or special techniques for preservation in viable form. The microfilariae do not reproduce themselves and, sooner or later, die. The adult worms have a limited life-span likely to be cut short by injuries in manipulation. Thus, passage from an infected to a clean host by inoculation or transplantation can have no more than a temporary value in prolonging a strain. Cyclical development through a vector is essential if a filarioid parasite is to be isolated from captive hosts infected in nature and then kept as a continuous laboratory strain passaged only through laboratory-bred, clean animals. In the several instances where a vector was known there were practical difficulties in breeding and handling adequate numbers of the verte- [illegible] wever, [illegible] *ns* and [illegible] *ti*, was [illegible] cotton- [illegible] a brief account [illegible] laboratory. Before going on to the main subject it is worthwhile noting that the vector proved to be unusual in not being one of the biting diptera.

2. Cotton-rat filariasis

Both the definitive host, the cotton-rat, and the intermediate host, the mite, were amenable to breeding and handling in the laboratory in large numbers. Several methods were soon devised for maintaining a strain by cyclical passage of the helminth through the mite-vector. Most of these involved mite-infested artificial rat-nests (Bertram *et al*, 1946; Hawking and Sewell, 1948; Scott, 1948; Scott *et al.*, 1947, Williams, 1948), and they were undoubtedly successful for the purpose. But certain biological features of the material encouraged investigations of a more critical quantitative kind. The adult worms, for example, occur in the pleural spaces and, in certain circumstances, in the peritoneal cavity of the cotton-rat. Female worms may attain a length of 17 cm. and males [illegible] 1946). The sheathed non-

rather than improved the position Mites have been almost consistently too heavily infected, despite very low densities of microfilariae in the blood of the donor cotton-rat. The underlying causes are not fully understood although environmental conditions during the infecting meal when the mites take up microfilariae certainly require to be controlled (Bertram, unpublished). The necessary

cotton-rat filariasis.

4. Simple Infections

Despite this fundamental difficulty, a good deal of data has been compiled (Bertram, 1947, 1950 b, 1953 a, Kershaw, 1949) from cotton-rats infected on only one occasion (one day) with small to moderately large numbers of worms, that is, up to about 50 worms of each sex We know, for example, that female and male worms

this relationship is somewhat erratic and, moreover, appears to hold good only for quite light infections, that is, up to about, say, 15 or 20 worms of each sex In these the blood infection may rise over

and could explain this disparity between the numbers of adult worms and the microfilarial counts as the adult worm burden increases beyond moderate numbers The largest counts of microfilariae in the blood stream occur about the seventh month of the infection and are followed by declining densities until few or no microfilariae

of periodic partial feeds over many hours before becoming replete is an additional factor, particularly since the density of circulating microfilariae in the host is subject to random fluctuations more or less continuously (Bertram, 1949).

The other problem is that of the failure of many of the parasites to reach the infective stage in the vector. This is, indeed, a phenomenon common to most, if not all, pathogens of animals cyclically transmitted by arthropods. It is a subject about which much remains obscure although different factors have been postulated, or proven, for certain parasites, filarioid (Bertram, 1950 a; Kartman, 1953; Lewis, 1953; Reid, 1953) or otherwise, and their vectors. [illegible]

clear, a better understanding and better control of the infections this parasite can cause in the definitive host and in the vector became, and still remain in part, more fundamental issues demanding first consideration. With this inadequate recognition of a fascinating general problem, let us return to infections of the mite as they affect quantitative transmission

In some early studies (Bertram, 1949) of nearly 1,500 mites positive for infective larvae most mites contained from one to five larvae but much heavier infections, up to 78 worms in a single mite, were not unusual. These heavily infected individuals restricted confidence in the reliability of estimates of how many worms would be transmitted by a known number of mites—about 10 to 30 mites—feeding [illegible]

then rare and most contained only one or two worms. Higher infection rates were coupled with the troublesome, heavily infected individuals In the experiments with lightly infected mites, agreement between estimated transmission to, and actual infections as [illegible]

rather than improved the position. Mites have been almost consistently too heavily infected, despite very low densities of micro-

efficient vector is not usually a source of displeasure to a parasitologist, but the excessive efficiency of this vector is from the quantitative point of view an undesirable aspect of the transmission of cotton-rat filariasis.

4. Simple Infections

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20 worms of each sex In these the blood infection may rise over

and could explain this disparity between the numbers of adult worms and the microfilarial counts as the adult worm burden increases beyond

By then, the adult worms may also be dead, and encapsulated. Thus, cotton-rats can outlive their infection if parasites are transmitted once only on a single day (Kershaw and Bertram, 1948) They will usually infect the vector throughout the course of their year-long infection so long as some microfilariae (at least 10 mf/cu. mm.) are

in the blood. In early experiments, they were rather better infectors about the seventh month of their infections, almost regardless of microfilarial density, than in earlier or later months (Bertram, 1950 a).

5. Infections following intermittent exposure to transmission.

The relationship of microfilarial density to adult worm numbers is, however, by no means so straightforward as has just been described When very large numbers of worms are transmitted on a single day (Bertram, 1953 a) most go, as usual, to the pleural cavity (for example, 301 females and 255 males) and a few (5 females and [illegible]

space were of normal length (mean = 11·3 cm.). Other observations confirm that quite few adult worms in the peritoneal cavity can contribute substantially to the numbers of microfilariae in the blood stream. There is, probably, another factor concerned. The highest count in the writer's experiments is 9,505 microfilariae per cu. mm [illegible]

the result of one short period of a few days' exposure to infection in an artificial rat-nest followed by a second similar exposure about four months later Here we have an indication that reinfection may be an important cause of heavy infections of both adult worms and microfilariae. Further observations (Bertram, unpublished) have confirmed that short periods of exposure to reinfection in artificial nests at intervals of several weeks or months result in the cottonrats harbouring quite large numbers of adult worms, some encap- [illegible]

successfully enough to add to, and maintain, high levels in the microfilarial density of the blood stream. Cotton-rats with in- [illegible] filarial count of 6,989 microfilariae per cu mm, although causing a 91·3 per cent infection rate in the mites with a mean of 19 9 infective larvae per mite and a maximum of 59 larvae in a mite, may not infect better than a density of, for example, 375 microfilariae per cu mm in another cotton-rat In the latter case, the infection rate was actually 95 5 per cent and the mean and maximum infections in a mite, respectively, 21 3 and 55 infective larvae (Bertram, un- [illegible] same batch (for example, from a recent batch, one to 98 infective larvae per mite) seems to ensure that some mites should survive. Such checks to adverse effects on the vector favour, of course, the prospects of the parasite's transmission.

6. Infections following prolonged exposure to transmission

There is, however, yet another aspect of the relationship between parasite, host, and vector under conditions of superinfection which must affect the efficiency of transmission If cotton-rats are exposed in artificial nests to a risk of repeated reinfection for continuous [illegible] becomes negative and remains so for months afterwards. At autopsy there are signs in the pleural spaces of absorption of calcified and encapsulated worms as well as some stunted live females (for example, 79 females of mean length 6 5 cm) and 109 small male worms [illegible] heavy, appears to inhibit severely growth and reproduction by adult worms in both cavities. When their blood is negative, such hosts must break the continuity of transmission They are, moreover, thin, lethargic creatures below normal weight and premature death is not unlikely. But, since not all the cotton-rats exposed to rein- fection for long continuous periods in these laboratory-induced

epizootics suffer so severely, or become completely negative for microfilariae, transmission can still continue within the host community One may speculate how in such circumstances [illegible] transmission. It is not supposed that such extreme swings are an inevitable cycle for host infections and the transmission rate in nature. Other factors, some of which can be conceived, may well stabilize a tendency to do so at some average level of infection and transmission more favourable to host and vector survival and, with that, the parasite's survival.

7. Conclusions

One realizes the complexity of the problem when it is appreciated that virtually unlimited permutations and combinations exist of the different frequencies with which different numbers of worms may be transmitted to a cotton-rat during a life span of, at least in the laboratory, up to about 3 years. Only two contrasting patterns of [illegible]

remain obscure Analysis and interpretation are correspondingly limited and difficult One feels that the limit has been reached in the usefulness of such methods and that further understanding of the significance of different amounts of reinfection will depend on controlling, and being sure of, the numbers of worms transmitted at each exposure As pointed out above, this simple requirement of precise quantitative transmission still remains, unfortunately, an elusive perfection. One may, however, sum up the available results from cotton-rat filariasis by saying that, apart from the susceptibility and efficiency of the vector, such characteristics of the infection in the cotton-rat as the numbers of adult worms, their sites of development, amounts and frequency of reinfection, and pathogenic effects are important biological variables affecting the course of the infection and, with that, the transmission of the parasite. The constant interplay of all these factors appears to ensure the survival of the parasite as an organism although it also entails sacrifice of many individuals by their imperfect development or death in the cotton-rat and in the mite apart from losses from the deaths of the hosts themselves.

The extent to which this kind of research may be thought to enlighten problems in human filariasis has been discussed elsewhere (Bertram, 1953 a, 1955). This sphere of comparative thought is not, I think, wholly unrewarding although it must be entered with a great

deal of caution It may be sufficient to emphasize one aspect of the matter here. The remarkable biological differences between the several human filarial parasites at once indicate the need to investigate more than one kind of animal filarioid infection Whether suitable filarioid parasites in animals or birds exist in a pathogen-host-vector system which will submit to laboratory maintenance and be at least as convenient for comprehensive study as cotton-rat filariasis, remains for the future to reveal Although it may be expecting too much from nature, infections with much shorter time factors than those of cotton-rat filariasis would be an inestimable boon The present paper on cotton-rat filariasis, an infection unique so far in its opportunities for laboratory research with this kind of arthropod-borne parasite, may have its value not only as an account of biological facts and factors controlling the transmission of this particular parasite but also as a general statement of desirable characteristics in materials for experimental filariasis and of some problems which await investigation in this field

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THE EVOLUTION OF SOME ANIMAL VIRUSES

By

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IN discussing the evolution of animal viruses we do best to ignore or by-pass the controversial topic of their origin—whether from larger microbial parasites or from errant animal genes Let us

animal poxes, something originally caught from man's domesticated livestock. There is ample evidence that a virus indigenous to and well tolerated by one host may be carried to a strange host in which

the tropics, transmission by arthropod vectors appears to be the

of infection. New viruses may at this time have replaced the old, or old ones may have learnt to travel in new ways.

An example of the latter tendency seems to be afforded, not by a

infection occurs amongst cattle through other channels, perhaps inhalation of dust; and that human beings contract infection through drinking milk from infected cows or by other close contact with cattle. Tick-borne meningo-encephalitis, due to a virus related to louping ill, occurs in eastern Europe; it is suggested that this infection may be transferred at times by means of dust or milk (Richling, 1955)

An interesting example is afforded by myxomatosis of rabbits.

to be naturally transmitted by insect bites, mosquitoes being particularly involved. As is well known, myxomatosis has been introduced into Australia and Europe where it has wiped out millions of European rabbits The Australian workers have maintained that transmission is purely mechanical, through the bites of all sorts of arthropods, especially *Anopheles* and other mosquitoes, but also of black flies (*Simulium*), stick-fast fleas (*Echidnophaga*), in fact anything with a proboscis which can act as a " flying pin ". Work by Kilham and Dalmat (1955) in the United States on the related fibroma virus suggests that multiplication within mosquitoes should not be too hastily excluded Similar doubts arise as the result of work in

well see, *in this instance*, how *modification of the properties of* myxoma virus could readily avail to allow it to change over from being normally insect-borne to transmission by contact or even through the

When poxes, we find it generally recognized that -borne. It is usually assumed that here

also transmission is only mechanical French, however, has recovered fowl-pox-like viruses in the field from wild-caught mosquitoes Further, Bos (1934) has found *Anopheles* still infectious 210 days after their infecting feed. Virus originally present in various parts of the insect has later been present only in mouthparts. As with myxoma, doubts arise as to whether multiplication in the [illegible] form a natural group, it is hard to believe that transmissions—by insects and otherwise—are different techniques existing side by side for aeons far likelier than one has evolved from the other within relatively recent times.

It is generally agreed that mutual tolerance by host and parasite is a hallmark of successful parasitism and is commonly an indication that host and parasite have been living together for a very long time. Violent reaction leading to death of the host cannot as a rule help the parasite to become widely disseminated and successful. Let us apply this criterion to the virus infections in which two hosts—a vertebrate and an arthropod—are concerned Which is the primitive host? Where did the virus start? Did viruses "begin" in insects and make use of vertebrates as a means of getting from one insect to another? Or was it the other way round did vertebrate parasites make use of arthropods as a means of getting about? Viruses can hardly have been able to grow in both sorts of creatures from their very beginnings unless of course they have evolved from arthropod-borne protozoa—a conclusion which merely pushes the problem a little further back in pre-history A number of animal viruses are known to multiply both in the vertebrate host and in the arthropod vector No such virus is known to do any harm to the insect in which it grows, while many cause illness in vertebrates. On this reasoning, viruses are more likely to have originated in insects and other arthropods Such an origin has indeed been [illegible]

viruses may kill human beings and horses but their natural vertebrate hosts are probably birds, in which they produce little harm. [illegible]

of infection. New viruses may at this time have replaced the old, or old ones may have learnt to travel in new ways.

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through the air

When we turn to the other poxes, we find it generally recognized that fowl-pox is often insect-borne. It is usually assumed that here

[illegible] apparent that a virus had ever been concerned. In fact a latent virus can only be demonstrated to exist where integration is incomplete and some stimulus acts to upset a host-virus equilibrium (Andrewes, 1952).

Traub (1939) has described studies of a colony of mice in which infection by lymphocytic choriomeningitis virus was endemic Infection was at first spread by urine and other means but later came to be transmitted *in utero*. Young mice infected thus were tolerant of the virus, finally all were infected but showed no signs at all that this was so A virus infection transmitted by excreta had been trans- [illegible]

The second, excreta-borne, stage may in some instances have been omitted. Transfer of infection from one host to a strange one may often have initiated a new cycle This would most often be apt to [illegible]

helpless host

While the pageant of metazoon evolution moves so slowly that we can hardly detect its progress, virus diseases seem to be appearing, waxing and waning within the lifetimes of human observers.

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[illegible]

of a virus before we dare speculate very far as to origins.

It should be mentioned here that some plant viruses are known to multiply in their insect vectors—homopterous bugs or leaf-hoppers (Black, 1953) They are probably harmless to these insects and are at least much less so than they are to the plants. Can we envisage an insect origin for plant viruses also? Bawden (1950) has suggested this possibility. Can we conceive that as some animal viruses have [illegible]

their further spread.

The purely insect viruses aptly illustrate the third main method of transmission of virus infection, termed by Gross "vertical transmission". *This he contrasts with "horizontal transmission"* to the host's neighbours; he implies passing on, perhaps in the ovum, to the next generation The method is by now a fairly familiar one. In the case of the virus diseases affecting caterpillars, the disease [illegible]

newly-hatched larvae (Smith *et al*, 1953) Bittner's milk factor causing mammary cancer *in mice is transmitted particularly by* [illegible]

normally occurs by hereditary channels, not in this instance through the milk.

PROPERTIES OF SOME INFECTIVE AGENTS IN RELATION TO THEIR MODES OF TRANSMISSION

By

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[illegible] it is exposed to by the mode of transfer from host to host that it ordinarily uses It might therefore be of some interest to consider some of these properties in relation to the common means of transmission.

Ability to survive apart from the host

The most resistant micro-organisms are the spore-forming [illegible] eradicate because the organism survives for long periods in the wood of animal houses and yards) It seems that parasites whose survival is provided for adequately by their capacity to form resistant spores are seldom if ever endowed with a high degree of infectiousness [illegible] invaders to dwell long on a mucosal surface, for example. In the second place spores are not endowed with any offensive weapons, such as vegetative organisms often have (e g toxins, hyaluronidase, leucocidin) nor could they very well have attachment mechanisms, enzymic in nature, as have, for example, viruses of the influenza group.

On the other hand some agents causing highly infectious diseases are not able to survive for long periods apart from their host, the viruses of human influenza, swine fever, for example Some of the viruses and protozoa transmitted by arthropods are particularly delicate as also is the syphilis spirochaete and the gonococcus whose

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enormous numbers and if there are sufficient susceptibles in the population the epidemic will spread with great rapidity; if this does not happen the infection disappears (possibly surviving in the occasional carrier)

On the other hand, the long lasting diseases—leprosy, tuberculosis, virus pneumonia of pigs, trachoma, foot-rot of sheep, are much less infectious Evidently the infective agent is either shed in fewer numbers or it cannot so easily initiate infection in the new host and quickly spreading epidemics do not occur The parasite is shed over [illegible]

only one of the following means.—

(i) capacity to survive for a long time apart from its host;
(ii) persistence for a long while in the host, with continuous or intermittent shedding,
(iii) a high degree of infectiousness for a short period, usually coupled with some other means of survival, such as occasional carriers or a reservoir host

We have already discussed the reasons why means (i) tends to be incompatible with means (iii).

The reason why (ii) and (iii) tend to be incompatible is probably that a high degree of infectiousness probably requires the shedding of large amounts of virus and this is only likely to occur when there is [illegible]

interfere with the shedding of the virus in an infective form. In long-lasting infections the parasite may not be shed continuously but only when a [illegible]

General variability of parasite

Some microbial parasites appear genetically very stable while others are subject to variation of several properties, including the

tion in animals and plants

It is to be noted that agents that spread by the airborne route, such as influenza and foot-and-mouth virus, may not appear particularly resistant under certain conditions in the laboratory so

survive under the circumstances normally encountered in their transmission from host to host

Another illustration of this principle is seen with the non-sporing Gram negative anaerobes, such as *Fusiformis necrophorus* and *F. nodosus.* In pure culture they are quickly destroyed by exposure to air but under natural conditions they are nearly always associated with aerobic bacteria, such as Staphylococci or coliforms. These latter afford protection to the air-sensitive anaerobes. The mechanism of this protection has not been fully investigated but there are probably two factors involved. The aerobes produce catalase which prevents the anaerobes from destroying themselves by the production of peroxide They also maintain a strong reducing potential even in very thin layers, such as the moist surface of an ulcer.

There is often considerable discrepancy between the resistance of a parasite to conditions met in the laboratory and its resistance under the conditions it encounters in nature. In the examples cited above the parasite does better under natural conditions than in the laboratory but this is not so with all parasites Swine fever virus

discrepancy is not thoroughly understood but it is thought that the poor survival under natural conditions is due to the virus being quickly destroyed in putrefying material.

Degree of infectiousness

This property is difficult to define precisely or to measure but it

the infective agent are highly infectious. The parasite is shed in

in the blood stream or skin Airborne infections are mostly spread from the respiratory tract The rabies virus multiplies only in the central nervous system and the salivary glands, the latter localization obviously being necessary for a parasite that is dependent on biting for transmission—the biting incidentally being ensured by the effect of the virus multiplying in the brain on the behaviour of the animal. Subjectively speaking, we may regard this as a beautiful biological adaptation or a diabolical one, depending on our point of view.

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following: antigenic characters, virulence, host adaptation, "p–q" phases. These properties do not lend themselves to discussion in relation to modes of transmission except that the p–q variation calls for some comment in this connection since it is thought to be associated with epidemic behaviour of the agent.

The attractive hypothesis has been put forward by Isaacs and Andrewes (1951) that the influenza virus survives inter-epidemic periods in the
the presence
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is much more
antibody. There is some evidence that also infectious laryngotracheitis and possibly other viruses can exist in theses two phases

Transmission over long distances

Certain plant diseases, e g rust, are said to be carried 1,000 miles or more through the air. On the other hand, animal airborne diseases are generally believed not to be transmitted more than a few yards at most in the open air. Perhaps this difference is related to the need, since plants occupy fixed positions whereas animals move about and so are able to come in close contact with one another But there are at least two animal diseases, foot-and-mouth and

occur in the southern border of Norway cannot be explained on this basis and the only apparent explanation is that the virus is carried as droplet nuclei by the wind 100 miles from Denmark. The foot-and-mouth disease virus has properties which might enable it to travel further by air than other animal viruses: (1) it is shed in large amounts from the infected animals, many of which are usually affected at the same time, (2) it is able to survive for a considerable time in the dried state, (3) it is extremely small, (4) it has an exceptionally high degree of infectiousness

Mode of transmission in relation to character of diseases

THE DISSEMINATION OF PLANT DISEASES AND PESTS IN INTERNATIONAL PLANT TRADE

By

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Most pests and parasites have remarkable powers of reproduction, but apart from some insects which are able to fly long distances, they depend for more than local natural spread on external agencies such as wind, water and animals It is believed, for instance, that black rust of wheat sweeps northward on the wind from Texas to Canada every year, and that winds can carry the spores of white pine blister rust several hundreds of miles. But though many insects and fungi may be disseminated in this way, the journey is often hazardous, with mountains, deserts and oceans frequently providing natural geographical barriers, and climate or unavailability of host plant very greatly reducing the chances of establishment in new territories Few species have a wide host range and even the hosts have their habitat limitations Pests may also be carried passively in ships, trains or aircraft, but at the journey's end they still need to find their [illegible]

[illegible]

This is reflected in many of the names applied to them We talk of the American gooseberry mildew or Dutch elm disease, while in America we hear about the Japanese beetle or European corn borer, and are told that well over half the damaging crop pests there have been introduced from other parts of the world. The literature is full of descriptions of newly introduced pests or diseases, often with nicely tabulated time-tables of their successive appearances

listed as immune and widely grown. With most other parasites no such criterion of immunity is possible and there is little likelihood of detecting new strains of them until it is far too late to give any hope of exterminating them

One other way in which new introductions can take place deserves special mention here The practice among research workers in different countries of exchanging fungus cultures and diseased

prevent new introductions by legislation, and it is not surprising that different countries adopt very different policies about plant importations. Some of these differences are inevitable and understandable Island countries, or countries protected in part by natural geo-

process of agricultural development, or where thousands of acres may be devoted to a single crop or even a single variety, for it is under such conditions that epidemics spell disaster Mainly export-

solution in complete embargo wherever this can be resorted to without appreciable damage to domestic economy i e embargo based on self-sufficiency. A better guiding principle, and one that is implicit in the F A O Plant Protection Convention of 1951 and is

This is the principle accepted in the United Kingdom and it underlies the 1955 Importation of Plants Order made by the Ministry of Agriculture, Fisheries and Food, which governs the entry of agricultural and horticultural plants and parts of plants into England and Wales Similar Orders apply to Scotland and Northern Ireland. Under these Orders many raw vegetables and fruits are allowed unrestricted entry, a few plants are prohibited altogether, and all

for instance, was undoubtedly introduced into this country during the Second World War with infected seed imported from a country where the disease is widely distributed. But by and large a pest or disease that does find a footing in a new country is rarely noticed until it causes appreciable damage, and it is then usually too late to trace its origin accurately. Moreover it is surprising how frequently evidence for the origin of a new pest or disease is upset by subsequent discoveries of earlier records. Wart disease of potatoes was originally described in 1896 in what is now part of Czechoslovakia. The temptation then, as now, was to relate subsequent discoveries to the earliest one. So that when wart disease was found in Cheshire in 1900 the inference was made that somehow or other it had reached us from central Europe. Yet

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disease may lead to its establishment, the normal wastage must be

other reasons.

Sometimes a newly introduced pest or disease makes great headway during the first few years and then settles down as a not too troublesome native. Among diseases of this nature that created a great stir when they arrived in this country were hollyhock rust (1873), chrysanthemum rust (1897), American gooseberry mildew

it in good faith and therefore rely to a large extent on the goodwill and integrity of the phytopathological service in the exporting country, for only 1–2 per cent of the consignments entering the country are check-inspected to test the validity of the certificates issued. On the other hand we take more stringent measures to protect ourselves against particular diseases, or diseases of particular crops, and these extend even to prohibition in a few instances. It is extremely difficult to assess the real value of the Importation of Plants Order in keeping out unwanted pests and diseases, and just as difficult to judge the potentialities of those that undoubtedly slip through from time to time. But there is no doubt whatever that for over twenty-five years we have successfully resisted the invasion of Colorado beetle, despite its prevalence on the Continent, and this can justly be attributed to the restrictions placed on imported produce, for certain temporary relaxations in the import of fresh [illegible] to the co-operation of the general public in reporting the finding of the isolated beetles that do, in fact, arrive here annually on ships and in imported produce

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other plants and plant products are allowed in provided they are [illegible]

safeguards about wart disease (*Synchytrium endobioticum*) and bacterial ring rot (*Corynebacterium sepedonicum*) The potato is a vital part of our national economy and these stringent measures are prescribed to prevent the introduction of ring rot and a number of important virus diseases unknown in the United Kingdom, including spindle tuber and yellow dwarf. The embargo is not absolute because provision is made under the Order for the importation of any restricted material under licence. Seed potatoes required for scientific or other worthy purposes can therefore be brought in under licence, to which all necessary safeguarding conditions can be attached.

The only other prohibitions are on imports of annuals, biennials, *Prunus*, *Rubus*, *Fragaria* and *Rosa* from those countries or continents in which there exist dangerous virus diseases unknown in Britain, such as aster yellows, curly top, certain stonefruit viruses and rose wilt.

Restrictions on the entry of nursery stock, bulbs, etc. are designed to meet two general aims. The first is to ensure that the importer is receiving healthy goods. Exporting countries are therefore asked to certify that the plants consigned to the United Kingdom were examined during growth and again just before export and were found to be substantially free from injurious pests and diseases. The second object is to avoid the introduction of Colorado beetle, San Jose scale and potato wart disease, and this is sought by laying down certain requirements about the place of origin of the planting material.

[illegible]

Commissioners.

Powers already exist under a domestic Destructive Insects and Pests Order to deal with any non-indigenous pest or parasite which [illegible]

THE POPULATION DYNAMICS OF THE FILARIAE OF MAN WITH PARTICULAR REFERENCE TO *LOA LOA* AND *ONCHOCERCA VOLVULUS*

By

W E KERSHAW

School of Tropical Medicine, Liverpool

we believe are first stage larvae (the nematodes undergo development,

referred to as the host-parasite-vector complex The fortunes of the

lower, or in extinction or in the precipitation of a new evolutionary venture

Consideration of the host-parasite-vector complex involving *L loa* and *O volvulus* is rendered difficult by uncertainty regarding the rôle of animal reservoirs of infection and, as Professor Gordon has pointed out, by our ignorance of many of the fundamental principles involved in the transmission of vector-borne helminth infections

In the case of *L. loa* we believe that the complicated and multiple host-parasite-vector complex involving *L loa*, man and several species of monkeys, and several species of the red fly *Chrysops*, is

night, and this feature is closely related to the biting habits of the principle vector of human loiasis, *Chrysops silacea*, which bites only during the hours of daylight The shape of the curves of the concentration of the microfilariae in the peripheral circulation and of the biting habits of the fly plotted against time are almost coincident

The manner in which the fly obtains its blood meal affects the prospect of its taking up microfilariae. Unlike the mosquito which has fine slender and flexible mouthparts, and may feed from a capillary or from a pool of blood produced by lacerating a capillary, it seems almost certain, though direct confirmation is lacking, that *Chrysops*, with sharp but more sturdy mouthparts, feeds only from a pool of blood The uniformity or otherwise of the distribution of microfilariae in the minute vessels which are lacerated, the ease with which the microfilariae may be retarded in their movement along the proboscis with the blood meal are all factors which may influence the intake

The intake of the microfilariae of *L. loa*

The actual intake of microfilariae may be compared with the expected intake as computed from the concentration of microfilariae in the peripheral blood as estimated in the sample obtained by pricking the finger and from the size of the blood meal ingested The number of microfilariae taken in by most flies is smaller than might be expected whether the expected number is large or small and only a few take in more No pattern can be seen in the relationship

Nevertheless, though there are individual variations in a group of flies, the actual intake and the expected intake of a group of flies are, under laboratory conditions, and probably under natural conditions, related Under certain laboratory conditions, they have a log-normal distribution, and using the geometric mean as a parameter, a group of flies feeding to repletion takes in roughly half as many microfilariae as would be expected

From the information derived under natural conditions in the field, from surveys of both the human population and of the insect vector coming to bite man, in which estimates of both incidence and intensity are used, it is possible to compare the population of parasites in the peripheral blood of man—the reservoir of infection to the fly—the developing forms in the fly, and the final form in the vector infective to man It is not possible in these conditions to compare the expected and the actual intake of microfilariae In the circumstances of transmission in a rubber estate at Sapele in Southern Nigeria, frequency distribution curves plotted from the numbers of persons in the case of the reservoir, or the number of flies and the intensity of infection with microfilariae or larvae, have a log-normal distribution with but minor variations The frequency distribution

From an empirical approach to the reactions of the parasitic complex as reflected by the differences in incidence of infection in man in different vegetative zones, and in the changes produced by village and town evolution and by plantation development, it is evident that the parasitic complex is very sensitive to changes in its environment.

In the case of *O. volvulus* the host-parasite-vector complex involves man (and possibly certain animals) and several species of the black fly *Simulium*. This complex has established itself in West, Central and East Africa and in Central America and the north of South America in very different vegetative environments associated with fast-moving streams and rivers, but since serious studies on the intensity of infection are but recent, we have little information on whether the infection is at its climax. From what little we know of the incidence and intensity of human infection, the complex is not so sensitive to changes in its environment as is that of *L. loa.*

The infection in animals with other species of *Onchocerca* is world-wide, but we do not know what relation these infections may bear to that in man

It is therefore not possible by an analytical approach to build up an accurate and comprehensive mathematical model for these infections at present, but, as Professor MacDonald has pointed out, "These (models) are not intended for the demonstration of fully understood happenings, but are scientific tools of great value in experimentation and research. A model shows how epidemiological characteristics would interlock if all the assumptions on which it is made were correct. Comparisons of such models with nature shows which of the assumptions are finally acceptable and which to be

[illegible]

understood."

We are largely ignorant of the relationship between the parasite

[illegible]

parable with that derived from the experiments of Bertram in filariasis of the cotton rat. We propose therefore to restrict our observations to that part of the life-cycle involving the taking up of the parasite by the vector, and its fate in the vector

Factors affecting the intake of the microfilariae of *L. loa*

The microfilariae are present in the peripheral blood of man in large numbers during the day and in small numbers during the

intensities are all log-normal, and by the comparison of the geometric means it is evident that the case of moderate intensity of infection is a better reservoir than the infection of l[illegible]

out" case)

In considering the life-cycle of those parasites which are transmitted by insect vectors it is tempting to try to correlate the effect of interference upon one particular factor in transmission. Such selective interference is, in fact, not usually possible, except perhaps in the artificial conditions existing in the laboratory, since in the field any interference affects more than one factor and alters the balance of many It is therefore much more realistic to consider the effects of interference in the parasitic complex as an integrated whole, even though an analysis of the importance of the individual factors involved may be misleading in our present state of ignorance reg[illegible]

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complex to changes in the environment—such as deliberate measures to control the infections—can be assessed most properly and most profitably

curves using the logarithms of the intensity of infection have the same shape, reproducing accurately the minor variations; the [illegible]

the infective form

Factors affecting the intake of the microfilariae of *O. volvulus*

In the West African form of the infection the microfilariae are present in largest concentrations in infections of light or moderate intensity in the skin of the ankles, the calves and the buttocks and [illegible]

out ") infection, however, when the skin of the ankles and calves becomes fibrosed, the microfilariae immediately under the surface of these areas become fewer, and the transmission changes from enhancement to suppression.

In addition to the pattern of the distribution of the microfilariae [illegible]

In an advanced (" burnt out ") infection the microfilariae, though equally numerous, are concentrated deeply in the dermis *S. damnosum* in obtaining its blood meal erodes the skin down to the superficial layer of the sub-epidermal connective tissue. Its intake of microfilariae is therefore dependent upon the concentration of microfilariae in this layer.

The intake of the microfilariae of *O. volvulus*

The number of flies biting on the ankle and calf is roughly the [illegible]

DISCUSSION

I would like to ask Dr Ainsworth whether, since few systemic fungus diseases appear to be primarily infectious, and each case is apparently derived exogenously from a common source, e g soil or plant debris, there is not the need for a new approach to the study of these diseases

G C Ainsworth Yes, I agree, and I think that the perspective has already changed radically This is leading to a more rational approach to such diseases as coccidioidomycosis and histoplasmosis

E J Moynahan The current medical view is that the superficial mycoses are caused by fungi nearly all of which are obligate parasites and few of which are free-living Most of the deep mycoses are due to soil saprophytes, which produce disease in the tissues when the opportunity arises —sporotrichosis is a good example of this The outstanding property of the dermatophytes is their capacity to digest and live on keratin, a substrate unattractive to most organisms because of its chemical "toughness" The problem here is to learn how they deal with keratin, and then find the biochemical links between the enzyme systems involved and those the organisms use in the free-living state (if any)

We have much to learn about the ecology of the mycoses, and Dr Ainsworth has drawn attention to some of the problems raised by a study of their geographical distribution, but the study of ringworm infections in a relatively homogeneous population like our own raises similar problems Why is ringworm of the feet and groins so much an infection of the adult male and why is conjugal infection so rare? Why do certain species confine themselves to certain sites, e g *Nocardia minutissima* to the axillae and groins, while *Malassezia furfur* is rarely found in these regions? This specialisation is difficult to reconcile with free-living forms whose transmission has only been surmised but rarely studied

Co-operation between the mycologist and his medical colleague in this field is to be welcomed, and perhaps the link will be forged by the microbiological chemist who discovers the technique appropriate to the study of the fungus *in vivo*

G C Ainsworth Possible clues to some of the host-parasite interactions mentioned by the last speaker are dealt with by Rothman, *Trans N.Y. Acad Sci*, Ser II, 12, 27–33, 1949

THE DISPERSAL OF PLANT BACTERIAL PATHOGENS

W C. Moore Why is it that most bacterial diseases of plants in Britain are of little economic significance? If rain plays a vital role in the dispersal of our indigenous plant-pathogenic bacteria, it seems strange

THE DISPERSAL OF FUNGI PATHOGENIC FOR MAN AND ANIMALS

H G Thornton. Dr Ainsworth stated that *Sporotrichum* has been shown to be pathogenic to some plants How specific is this plant infection as regards its range of host?

G. C Ainsworth It is not known. In 1932 in the United States Dr. Rhoda Benham was able to infect both carnation and rose buds with *Sporotrichum*

H G Thornton Dr. Ainsworth suggested that some skin-infecting fungi may be derived from soil If this is so one might expect isolates from different patients to belong to different and possibly recognisably different strains Is there any evidence that this is so?

G C Ainsworth The isolates from different patients do at times show "strain" differences, but whether the soil plays any part in determining *this variation is unknown*

H G Thornton The point has been made that skin-infesting fungi from soil must have a specialized nutrition as they are able to attack keratin I would however point out that keratin-attacking micro-organisms are common in soil, as is shown by the use of hoof-horn meal as a fertilizer.

W. C Moore There are wide differences between the systematics of plant-pathogenic fungi and that of animal and human mycoses Dr Ainsworth is one of the few persons who have studied both subjects, and he may perhaps be able to judge whether the differences are as real as they appear to be, or whether further study may show that dispersal from plants to animals and man occurs more frequently than is suggested from the literature

G C Ainsworth While at present it seems unlikely that some of the [illegible] of man and animals are closely related to plant pathogens

..

P K. C Austwick Dr Ainsworth's reference to the isolation of an [illegible]

which spreads freely through the soil as rhizomorphs, the probability of infection seems to vary directly with the size and inversely with the distance away of the infected root serving as a food-base

Jane Meiklejohn. The factor of starvation as a cause of death of fungi in soil has been grossly under-estimated Most biologists do not realize how little nutrient is available in soil compared with the amounts provided in culture media. Most organic compounds occurring naturally in soil are only decomposed with difficulty, and the easily decomposed compounds—sugars, etc—that find their way into soil when fresh plant material is introduced must only survive for a matter of minutes, as the competition for them is so intense. The ionic strength of minerals in the soil solution is also very low

Mary Noble. When plants are used for the soil-trapping of fungi, does the treatment of the roots by various disinfectants affect the ability of organisms to attack the roots?

S D. Garrett I cannot agree too strongly with Dr Meiklejohn's remarks, which go to the root of the problem in more senses than one Microbiologists have a perverse preference for complex hypotheses concerning microbial antagonisms, when simple competition for nutrients often provides a complete explanation To answer Dr Noble's question would require data that we do not yet possess

FUNGAL DISEASES OF PLANKTON ALGAE

G E Fogg I have always thought of the cell wall of a diatom as rather tough Does the fungus penetrate it directly, or enter through a pore, or between the valves?

J W G Lund The fungus enters through the valves.

BACTERIA OF VETERINARY IMPORTANCE

R. E. O Williams It seems to be fashionable to speak always of the three methods of transmission of respiratory tract diseases—by droplets, by droplet nuclei, and by dust—as if they were each distinguishable and

that we do not suffer economic losses to the same extent as those caused abroad by other bacteria, including *Erwinia amylovora* and *Corynebacterium sepedonicum* in North America and *Pseudomonas solanacearum* in tropical countries.

J. C. F. Hopkins. From considerable experience of wildfire of tobacco (*P. tabacum*) in S. Rhodesia, I can support Dr. Crosse's contention that weather plays a dominant part in the dissemination of the bacteria through a crop, particularly by means of rain splash. But it is necessary to distinguish between dissemination and development of the disease. The former is frequently brought about by transplanting seedlings which have become infected in the seed-beds, and a primary infection is set up throughout a land. Misty weather, unaccompanied by driving rain, may then accelerate development in the plant, giving the impression of an increasing spread of the pathogen. Even so the disease does not reach the destructive epiphytotic stage under these conditions. For the latter, extensive water-soaking of the leaves, which only seems to be brought about by heavy and driving rain, is essential, and is comparable to the experimental infection induced by the use of a powerful jet of water followed by atomising of the pathogen on the treated plant. The phenomenon appears to be identical with that which Dr. Crosse has described for cherry.

Mary Noble. Halo blight of oats is probably also present on the leaves and attacks more readily when tissues are damaged by frit fly and/or weather.

R. E. O. Williams. The suggestion that many of the bacterial pathogens of the leaves of plants are related to the non-pathogenic flora of the leaf has a clear analogy in the pathogenesis of infection in the human skin. *Staphylococcus aureus*, one of the principal skin pathogens, is clearly closely related to the normal commensal flora of micrococci, and is itself commonly found as a commensal on the skin; trauma can drive these commensal *Staph. aureus* into the tissues, where they are able to produce disease.

THE SOIL AS A RESERVOIR OF PATHOGENIC MICRO-ORGANISMS

H. G. Thornton. Can Dr. Garrett tell me approximately how far a fungus can spread through field soil to reach and infect its host?

S. D. Garrett. The more specialised parasites spread only through actual or proximate root contact. With others, such as *Armillaria mellea*,

P. Tate In cultures of some entamoebae (*E invadens*) cysts are formed while conditions are favourable for growth As these cysts do not excyst in the same medium, but do so when transferred to a new medium, there must be some factor present which inhibits excystation in the medium in which they were formed Has Dr Neal any information about the existence of such an inhibitory factor?

R. A Neal After inoculation of a sterile tube of culture medium with amoebae and their concomitant bacteria, the variation of oxidation-reduction (redox) potentials with time of incubation falls into a regular pattern The redox potential in the sterile medium has a positive value, which after inoculation rapidly falls to a low negative value This potential is then maintained for a variable period, followed by a rise to a positive value It has been found that amoebae of *E histolytica*, *E ranarum* and *E. moshkovskii* will only grow at low potentials and that the rise in potential is accompanied by encystation of amoebae, until, at positive values, cysts only are present. At intermediate redox potentials, both amoebae and cysts may be present Therefore, once cysts have been formed *in vitro*, they will hatch and produce flourishing cultures only if the potential is lowered to a suitable value It is possible, therefore, that the redox potential acts as an inhibitory factor.

[illegible]

The determination of the structure and properties of the egg shell of ascarids has been much easier to carry out than similar investigations with amoebic cysts owing to the much greater thickness of the egg shell As a result of a number of investigations it has been shown that the egg wall consists of three layers, chemically composed of protein, chitin and lipo-protein respectively

The protein and chitin layers can be removed experimentally and the survival of the enclosed larva studied These experiments have clearly indicated that the "chemical protection", as distinct from the "mechanical protection", is a property of the innermost, lipo-protein membrane. While the high degree of impermeability shown by this membrane offers an

well-established I should like to know whether there is any direct evidence of transmission of respiratory disease in animals by droplet nuclei, using that term for droplets small enough to remain suspended in air for some time and to be carried on air currents for more than a few feet.

C H. Andrewes. We have heard about different means of disease transmission amongst domestic animals. Is anything known about transmission amongst animals in the wild state? Do they keep close enough together for airborne transmission to be effective in the open? Does this method perhaps operate for social animals but not others?

W H. R Lumsden In connection with Dr. Andrewes' remarks on the lack of knowledge of bacterial diseases in African game animals, I might mention that in Uganda hippopotamuses are occasionally infected with anthrax and that small epidemics occur from time to time among natives who have consumed the flesh of infected animals As far as is known, no other animals become infected from the hippopotamus, because—except for the intervention of man—dying animals are probably eaten only by crocodiles

THE DISPERSAL OF PATHOGENIC AMOEBAE

Ann Bishop Is it known if there is any difference in the structure and composition of the cyst walls of *Entamoeba coli* and *E histolytica* which would account for the fact that the cysts of *E coli* can withstand drying, whereas those of *E histolytica* cannot?

R A Neal The cyst wall of *E histolytica* consists of one layer and measures about 0.5 μ in diameter, whereas the wall of *E coli* consists of two layers, a rigid, thick, inner wall, and a flexible, thin, outer wall, and measures 1.0 μ in diameter. Possibly these differences have some effect on the resistance to drying of the two species.

J. L. Harrison Dr Neal cites monkeys as possible alternative hosts of both *E histolytica* and *E coli*, but regards the transmission from

some instances these reports must be accepted with reserve Cross-infections appear to occur between pheasant and quail and, possibly, between sheep and goats.

R. A Neal. Are there serological differences?

C Horton-Smith We know very little about serological differences between species. Serum antibody seems to play little part in the resistance to re-infections developed by recovered animals although antibody is produced by hosts. Bachman failed to detect antibody in the serum of infected animals by the precipitin test, although its presence can occasionally be demonstrated by the complement-fixation test (Chapman, 1929). There is no cross-immunity between species, and this characteristic provides one of the criteria for their identification American workers have recently demonstrated agglutinins in the sera of experimentally infected chickens Second generation merozoites in suspension proved to be antigenic.

E L Taylor Are there really as many as six species of *Eimeria* occurring in the chicken? It always seems difficult to me to reconcile the high degree of host-specificity that is known to hold for these parasites with the occurrence of so many species from one and the same species of host.

Had they been less particular about the specificity of their hosts there would seem to be a possible explanation, in that at some time they might have come over to the chicken from some other species of avian host, but in view of the strict host-specificity it is difficult to understand, and I am [illegible]

C. Horton-Smith Dr Taylor's question is an interesting one, and at present we can only speculate on these matters As Dr Taylor knows, Tyzzer has laid down certain criteria for determining the specific status of a coccidium. these criteria are based on morphological and biological characters, such as dimensions and structure of oocysts, length of life-cycle, site of parasitism, sporulation time, and so on. The fact that no cross-fertilization and no cross-immunity occurs between the different coccidia within a host lends considerable support to the belief in their specific status On the other hand, some of the characters used by Tyzzer overlap different species, as, for example, the distribution of the intestinal species, the dimensions of the oocysts, the degree of pathogenicity, etc. All the coccidia probably have foci in which there is a maximum production of asexual forms, but extending from the foci of high parasitism are regions of decreasing parasitism which may, and often do, extend into similar regions of low parasitism by other coccidia. The

explanation of the great resistance ascarid eggs show to desiccation, it at the same time raises interesting problems concerning the hatching mechanism.

Recently the process of hatching has been closely observed by placing infective eggs in a few drops of intestine contents on a warm stage microscope. The behaviour of the larva changes within 15 minutes; instead of turning in all directions, the head is placed against the shell wall and the body moved rapidly to and fro. In from 30 minutes to 1 hour a small pore is formed through which the larva escapes.

This change in behaviour clearly indicates that some stimulus has been received by the larva from the intestinal contents. The result of fractionating the intestinal contents has not helped to elucidate the problem, as the property of stimulating the larvæ to emerge is easily lost. For example, filtration through collodion membranes or seitz filters inactivates the gut contents It is difficult to visualise a molecular structure able to cross the lipo-protein membrane yet unable to pass through a seitz filter.

I think that Dr Neal will agree that although the solutions of these two problems, the hatching of ascarid eggs and the excystment of amoebae, are unlikely to be the same, there is nevertheless a close parallel between the problems facing workers in both fields.

THE TRANSMISSION OF COCCIDIA

K. Mellanby. When the parasites have passed through a series of birds do they always possess the same qualities as they did at the start, or do they, like some trypanosomes, become more or less infective or different in virulence?

C. Horton-Smith. There are difficulties in assessing these qualities, [illegible]

R. A. Neal. Are the coccidia host-specific?

C. Horton-Smith They are usually host-specific Sporadic cross-infections between different species of host have been reported, but in

some instances these reports must be accepted with reserve Cross-infections appear to occur between pheasant and quail and, possibly, between sheep and goats

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E. L. Taylor. Are there really as many as six species of *Eimeria* occurring in the chicken? It always seems difficult to me to reconcile the high degree of host-specificity that is known to hold for these parasites with the occurrence of so many species from one and the same species of host

Had they been less particular about the specificity of their hosts there would seem to be a possible explanation, in that at some time they might have come over to the chicken from some other species of avian host, but in view of the strict host-specificity it is difficult to understand, and I am inclined to suspect that there may not be so many species as appears Could Dr. Horton-Smith perhaps suggest some way in which the multiplicity of species could be brought about during the course of their evolutionary development?

C. Horton-Smith Dr Taylor's question is an interesting one, and at present we can only speculate on these matters As Dr Taylor knows, Tyzzer has laid down certain criteria for determining the specific status of a coccidium· these criteria are based on morphological and biological characters, such as dimensions and structure of oocysts, length of life-cycle, site of parasitism, sporulation time, and so on The fact that no cross-fertilization and no cross-immunity occurs between the different coccidia within a host lends considerable support to the belief in their specific status. On the other hand, some of the characters used by Tyzzer overlap different species, as, for example, the distribution of the intestinal species, the dimensions of the oocysts, the degree of pathogenicity, etc All the coccidia probably have foci in which there is a maximum production of asexual forms, but extending from the foci of high parasitism are regions of decreasing parasitism which may, and often do, extend into similar regions of low parasitism by other coccida The

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C. Horton-Smith. There are difficulties in assessing these qualities, since an increasing resistance develops quite quickly in the host with increase of oocysts ingested. When oocysts are collected from one bird [illegible]

R. A. Neal. Are the coccidia host-specific?

C. Horton-Smith. They are usually host-specific. Sporadic cross-infections between different species of host have been reported, but in

division, we would have a tool for locating meiosis in organisms too small for conventional microscopic methods The fact that while these drugs do not prevent microgamete formation in *Plasmodium*, they do arrest immediately the first and subsequent divisions of the oocyst nucleus, may mean that *Plasmodium* displays gametic meioses in contradistinction to the majority of the Coccidiomorpha

C Horton-Smith When sulphonamides are applied to infected chicks at chemotherapeutical concentrations, inhibition of nuclear division in the schizogonous stage is usual Interference with nuclear division of the second-generation schizont is most pronounced The sulphonamides

susceptible to the action of sulphonamides than those of the first generation; this may be associated with the greater size of the second schizont and its greater depth of penetration, which brings it into closer contact with the vascular sub-mucosal tissues

THE TRANSMISSION OF HELMINTHS OF VETERINARY IMPORTANCE

Edward Hindle I have been struck by the very high mortality in the developing Trichostrongles—only one per 1,000 eggs reaching the third larval stage Can this be explained entirely on the supposition that it is the result of adverse external conditions, or are genetic or other factors involved? It is difficult to accept the view that in our damp and mild climate eggs developing in rich pastures should find the conditions so adverse as indicated by Dr Taylor's figures

E L Taylor I think that the explanation must lie entirely in the operation of external factors, largely on the delicate first- and second-stage larvæ Although strongyloid larvæ were known to be attacked by a variety of fungi in the soil I think it doubtful whether the activity of these parasites could be responsible for any great reduction in numbers

F. C Bawden Dr. Taylor states that the "ideal of parasitism is a balanced community in which host and parasite live happily together" I am less concerned at the moment by the difficulty of measuring the happiness of hosts or parasites than I am by the dangerous implication

coccidia in these regions of overlap may well be exposed to conditions that differ from those present in their normal focus of parasitism and become adapted to them, while the coccidia in the region of high parasitism, if we postulate a local immunity, will eventually be reduced in numbers, thus leaving a greater population of forms in the region of overlap, which may tend in evolution to parasitise this region more and more as time goes on Such changes of [illegible] immunity would be apparent between the more recently evolved forms and the original species from which they were derived. Arguing along these lines it might be concluded that the so-called species of to-day are sub-species of a single species At the same time, the phenomenon of host-restriction may have arisen among coccidia occurring in animals which are maintained in closed communities away from other species In this way it is conceivable that the protozoa become wholly adapted to a particular species of host Host-specificity may have arisen in coccidia of gregarious animals where there is a greater number of passages of oocysts through the same species of host within a given time than would occur in the case of oocysts of coccidia which inhabit the intestines of host species of solitary habit

Miss Clapham Which species of coccidia are responsible for diseases among pheasants and partridges? The results of infection resemble closely those found in poultry chicks infected with *Eimeria tenella*

C Horton-Smith The species of coccidia reported from pheasants are *E dispersa*, *E langeroni*, *E pacifica*, *E phasiani*. I can only recall the name of one species reported from partridges, *E procera* There have been several reports that *E tenella* from domestic fowls has been successfully transmitted to pheasants but they require confirmation I have failed to infect chicks with oocysts from pheasants *E. dispersa* occurs also in quail, but oocysts recovered from quail have failed to infect pheasants, but those from pheasants have infected quail Dr. Clapham says that the result of this coccidial infestation of pheasants resembles that in poultry chicks affected with *E tenella* *E phasiani* invades the cells of the lower small intestine and caeca, but the infestation does not appear to give rise to a condition at all comparable with acute infestations of *E. tenella* The whole question of cross-infection should be reconsidered and the species of coccidia occurring in British game birds should be determined

R. S. Bray. Are the inhibitors of nuclear division, such as sulphona-

micro-fungæ that parasitise the free-living larvæ of strongyloid worms and there is a French monograph by Dollfus of some 500 pages on the subject

THE DIRECT TRANSMISSION OF DISEASE

R. E. O. Williams It is worth stressing how little evidence there is, *apart from Professor Cruikshank's own single successful experiment, that* the bacterial respiratory tract diseases of man are in fact ever spread by way of infected dust particles I think that belief in the importance of dust arises from the great ease with which, for example, haemolytic streptococci can often be found in large numbers in the floor- and bedding-dust of hospital wards and barrack rooms Nevertheless practically all attempts to show that these reservoir are significant in the transfer of infection have failed

C. H. Andrewes The studies of my colleagues at Salisbury on the common cold virus indicated that infected fomites such as handkerchiefs were *relatively poor transmitters of infection Handkerchiefs of cold* sufferers were dried in the air and given to normal persons to use, colds did not result In conformity with this it was found that infected secretions painted on the outside of the nares failed to infect

Could the abrupt peaks of measles outbreaks be accounted for if a very small number of virus particles were needed to infect, and the flatter curves of whooping cough outbreaks by the need for a rather heavier dose of infection?

R. Cruikshank In reply to Dr Williams' comment, while I agree that recent evidence has been remarkably unsuccessful in incriminating strepto*coccus-contaminated dust as a means for spreading streptococcal infec*tion, there seems little doubt that the most dangerous reservoir is the heavy nasal streptococcal carrier As he disperses his streptococci mainly by gross environmental contamination, it seems likely that dried or partially dried particles from contaminated clothing, bedclothes, etc , would play their part in the spread of this infection. Factors such as the nature and dosage of the organism, the degree of drying and the susceptibility of the host tissues must all be taken into account in assessing the importance of dust-borne infection

In answer to the question raised by Dr Andrewes, I can only say that clinical experience indicates that the spread of whooping cough is facilitated by close contact *Against the hypothesis of this being " air-borne "* like measles is the finding from the Southall School trial with ultraviolet

that evolution strives to follow a pre-determined course, a sort of ever-improving welfare-state, and that host and parasite will inevitably first be antagonistic and then " learn how to live together satisfactorily ". Ideals are subjective, and their subjectivity when applied to evolution is simply illustrated by the conversation between two donkeys in a fly-infested field. One said, " How kind of Nature to provide us with tails ", and the other commented, " I would willingly have settled for no flies and no tail ".

Of course many examples could be quoted, that seem to fit with Dr Taylor's thesis, of parasites that caused lethal diseases when they first encountered hosts in which they are now less virulent But there are, too, plenty of examples of parasites becoming more virulent; the history of

host? Does a species gain or lose by prolonging the life of infected individuals so that they continue for long periods to provide sources of infection for other individuals?

Some parasites that now do little or no harm to their hosts may have reached the current state of near commensalism because of a protracted association during which a series of changes has progressively decreased pathogenicity. But commensalism is no sure guide to the length of time a parasite and host have been evolving in association When three different kinds of plant that have never been exposed to a virus are infected with it for the first time, one may be killed, the second suffer a moderately severe disease, and the third grow unhindered, although the virus may multiply equally in all three

warranted prescience when we assume that we can predict the direction of the change.

Edward Hindle. Are helminths themselves free from parasites?

These results suggest that tick-transmitted virus, were it not for the accident of the concurrent transmission of T B F, would usually be classed as a virus of the blood and spleen Two possibilities are suggested by this

A The disease is essentially a low-incidence nervous affection, transmitted to man and animals by some non-tick means (possibly via the respiratory or intestinal tract), which circumvent the blood-brain barrier In Britain circumstances have so developed that ticks can infect the nervous system of sheep via the blood, and tick-bite has now become the principal means of transmission to sheep, i e the vector method has supplanted the original, in the special case of sheep on tick-infested pastures

Against this theory are the objections that (1) there are no records of the odd case in tick-free areas, i e, transmitted by the original non-tick means, (2) pathogenesis studies suggest that there is essentially a humoral phase preceding multiplication in the C N S, (3) according to Andrewes' theory, this reverses the usual order, vector transmission being more primitive than other means, (4) with humoral infection only there is better tolerance, suggesting a more long-standing association

B The alternative hypothesis is that the L I virus is essentially not neurotropic Under British sheep-farming conditions it has become adapted, through the accident of concurrent T B F infection, to nervous tissue When the C N S is invaded, a special syndrome results, which is now regarded as characteristic, but which is basically an atypical reaction, by an alien habitat, the (possibly more common) reaction to bloodstream infection being less spectacular

There remains unexplained, however, the increased infection rate, in presence of tick-borne fever

Incidentally, L I has not to my knowledge been shown to be transmissible transovarially In my own work, negative results were obtained in 16 experiments I do not regard these experiments as conclusive, for various reasons, but the finding is supported by the consistently negative results reported by Alexander and Neitz with the L I virus in *R appendiculatus*

B W Lacey The mechanism of transmission of infective agents in ticks is of considerable interest Transovarian or transoval transmission is, of course, well established with many organisms besides viruses Yet in all of these the role of the male is almost unknown Thus invasion of the tick ovum by *Babesia bigemina*, with subsequent multiplication in the salivary gland anlage (Dennis, 1931), and infection of the ovum by *Brucella tularense* (Parker and Spencer, 1926), are recorded without mention of the male Similarly, the relapsing fever spirochaete has been seen in the egg, apparently multiplying (Koch, 1906), and the egg may be infective even in the absence of visible spirochaetes (Hindle, 1911), but the infectivity of tick spermatozoa is unknown Even in the human the comparable situation is not clear the spirochaete of syphilis has been

light that the incidence and spread of this infection were not affected by ultraviolet light irradiation, in contrast to measles and chickenpox

R. E Hope-Simpson It might be significant that in measles the virus particle enters through conjunctival tissue, whereas this is not the case for whooping cough

THE TRANSMISSION OF VIRUSES TO VERTEBRATES BY ARTHROPODS

J MacLeod. The virus of louping ill is classed as neurotropic Yet it is transmitted by a bloodsucking arthropod Whatever the method of transmission of the related R S S E. and Czechoslovakian diseases, there *is no doubt that in Britain natural transmission is by the tick.*

How then does the virus pass the blood-brain barrier, to gain access to its predilection tissue? Or is it possible that the virus is not essentially neurotropic, although its manifestation in sheep in Britain is often a nervous affection? The following unpublished evidence, though too scanty to be conclusive, is interesting

Excluding experiments on transovarial transmission, and *early experiments* where the evidence is doubtful, 35 sheep were tested with female or nymphal ticks infected experimentally with louping ill virus. In some of these sheep a concurrent infection of tick-borne fever was produced. The tick-borne fever agent causes a temperature reaction only, there are no symptoms of nervous affection, and the sheep almost invariably recovers.

	L I Infection	C N S Involvement Total	Death	Re-covery	Blood infection only Total	Death	Re-covery
L I. only	13 cases out of 21	0			13	3	10
L I.+T B F	*12 cases out of 14*	*8(9?)*	*6*	*2*	*4(3?)*	1	3

(" Blood stream infection only " means a temperature reaction with L I virus present in the blood, but no nervous symptoms, and no virus recovered from C.N S of those which died.)

It should be noted that there is a smaller mortality rate in non-nervous cases; that there is an increased L.I. infection rate from tick-bite, in the presence of T B F., that T.B F. is necessary for C.N.S involvement following tick-bite

W. H. R. Lumsden Might I draw attention to recent work in Uganda on the epidemiology of yellow fever where the work has been related to galagos? It has been known, since the work of Smithburn in 1942, that individuals of *Galago* spp in the field are frequently found "immune" to yellow fever in the ordinary neutralisation test There seems to be no reason to doubt the specificity of this test; Smithburn challenged some naturally immune individuals in his original work and found that they did not circulate virus. Some further recent work has given the same result in an immune individual challenged with asibi virus no circulating virus could be detected either by inoculation in mice or in galagos

It has long been considered that the infection of galagos with yellow fever by the ordinary route—by the bite of mosquitoes—was unlikely, for the following reasons The animals are strictly nocturnal and are active throughout the night, and so are not likely to be attacked much by nocturnal mosquitoes They mainly live in arid environments where, in the daytime, conditions of high temperature and low humidity generally result in minimum mosquito activity Attention has been attracted, therefore, to other blood-sucking parasites of the galagos The galagos rest in dry tree-holes, in nests of leaves, or on bare branches, and support a variety of such parasites That the infection is associated with the nests of the animals is indicated by some recent results of Haddow. In a sample of 45 *Galago senegalensis* distributed over 50 miles of road in Karamoja, Uganda, twelve were immune to yellow fever All these immune individuals occurred in one short 8-mile stretch of road, and all the others were non-immune There were four groups of more than one animal, in one group of four all were immune, in one group of three all were immune, and in another two, in a pair both were immune Confirmation is needed, but the data do encourage the study of the parasites associated closely with the animals or their nests The animals, or their nests, in different localities, may be infested with ticks, trombiculid and mesostigmatid mites and with lice Sandflies, common in hollow trees, should also be kept in mind At present several of these parasite groups have been passed over on purely circumstantial evidence, for instance, some of the heaviest infestations with ticks and trombiculid mites and lice have occurred in populations in which yellow fever immunes were not found At present work is being concentrated on the mesostigmatid mite *Liponyssus galagus*, which is a common nest parasite in an area where immunes are common These mites, of very

attempted

The occurrence of congenital transmission of St Louis virus has been mentioned by Professor Dick and such a mechanism might well explain the persistence of virus in inter-epidemic periods It is greatly to be

seen in the ovum (Lavaditi and Sauvage, 1906) and transmitted to dogs by injection of semen microscopically free of spirochaetes (Uhlenhuth and Mulzer, 1913), but, although obviously transmissible venereally, I know of no recorded instance—of congenital syphilis with an uninfected mother—which would indicate direct infection of an ovum With rickettsiae in ticks this possibility seems much nearer: the organisms have been seen in both ova (Gear and de Meillon, 1941) and spermatozoa (Wolbach, 1919), eggs have retained infectivity during five washes (Blanc and Caminopétros, 1932), and in copulation the male may infect the female and occasionally the female the male (Philip and Parker, 1933) It would be of interest to know if the colorado tick fever virus, or other transovally transmitted virus, is transmissible by semen, and, if so, whether it can infect the zygote without infecting the female parent

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Philip, G. B and P[illegible]
Uhlenhuth, P. and [illegible]
Wolbach, S B 1919 *J. med Res.*, 41, 1

C H. Andrewes. It may be very hard to decide whether a virus is multiplying in an insect vector. For viruses such as yellow fever it is suggested that only a small number of particles taken in by the insect will multiply; thus for multiplication to occur a big dose must be taken in The die-away rate of non-multiplying virus particles is fairly rapid. Thus one can readily demonstrate that virus taken up by a mosquito quickly falls off in titre and then rises again, though perhaps hardly above its original level.

Fenner and his colleagues maintain that myxomatosis does not multiply [illegible] that the related [illegible]

external contamination of the eggs, and the viruses are probably too unstable to survive for long except in living cells Whether these viruses occur in the gametes is unknown, but they seem not to enter spermatozoa, for the progeny between infective males and virus-free females are free from virus

I should perhaps stress that the great majority of plant viruses are not transmitted through the eggs of their vectors Similarly most are also not transmitted through the seed set by infected plants The few that are seem to enter the gametes and they have been detected in both the pollen and ovules

THE TRANSMISSION OF PLANT VIRUSES BY INSECTS

F C Bawden No plant virus has been found to have any deleterious effect on its insect vector, and infective insects seem to live as long and breed as freely as those free from virus On the contrary, the only effects that have been recorded might be construed as beneficial Leafhoppers raised on celery or aster plants infected with aster yellows virus have been reported to produce more young, to pass through the nymphal stages sooner, and to live longer than those feeding on healthy plants Similarly, aphids have been reported to be more fecund on virus-infected than on healthy sugar beets Whether the increased fecundity and other effects are caused by the viruses acting directly on the insects is doubtful, more likely the diseased plants contain greater amounts than healthy plants of substances that affect the insects' development, but, whatever their cause, the effects seem likely to favour the spread of the viruses

Another feature that could be significant in encouraging the spread of aphid-transmitted viruses is that probably the most common effect of viruses on plants is to make them turn yellow, and yellow is the colour that attracts most aphids

W. E Kershaw Could Mr Bawden say something about the specificity of aphids and plants?

F C Bawden The tissues on which insects feed can be very important in determining whether or not vectors become infective, and the differential distribution of viruses in different tissues can affect their transmissibility by insects For example, Mrs Watson several years ago discovered the odd fact that many viruses are more likely to be transmitted by aphids that are made to fast before they feed on an infected plant than by those that have been feeding continuously The proportion of aphids that transmit is only increased by fasting provided the time they feed on an infected plant is also brief, not more than a few minutes, prolonging the length

desired that the significance of such transmission should be more thoroughly understood. In this connexion also one should keep the sandflies in mind, for although Professor Dick quoted Sabin and his colleagues as coming to the conclusion that the congenital transmission of sandfly fever virus in sandflies was at most a rare event, there is some Russian work in which the reverse was claimed to be the case.

P Tate. The analogy between a "flying needle" and an insect with piercing mouth parts does not take into account that the insect's mouth parts are flushed with complex salivary secretions If such secretions were deleterious to some viruses it might explain why a virus may be transmitted by the prick of a contaminated needle but not by the puncture of an insect's contaminated mouth parts

F C Bawden I fully agree that to regard an insect vector as the equivalent of a "flying needle" is very misleading With plant viruses it would be quite wrong, for many of the viruses that are most easily transmitted by needles are not transmitted by insects that feed by sucking plant juices, although these transmit viruses less readily transmitted mechanically. There obviously is some very specific mechanism in an aphid's mouth parts that determines whether it transmits a given virus (or even one strain of a virus), but whether this specificity is set by salivary secretions or by the constitution of the mouth parts is unknown.

D S. Bertram In the medical and veterinary field it is a fact that,

F. C Bawden There is no doubt that rice stunt and clover club-leaf viruses are transmitted through the eggs of their leafhopper vectors Transmission this way seems too regular a process to come from a chance

trypanosomes follow the complicated route in *Glossina* generally accepted by protozoologists?

R. M. Gordon Dr Hoare said that developing trypanosomes of the *T brucei* group first multiply in the mid-gut and later "they migrate forwards into the proboscis and thence—*via* the hypopharynx—into the salivary glands". May I draw attention to the fact that this statement implies that each individual trypanosome must pass from the tip of the labrum to the tip of the hypopharynx, and ask whether any further evidence on this point is now available?

C A Hoare I agree that there are no records of direct observations on the passage of trypanosomes of the *Brucei* group through the hypopharynx, before they invade the salivary glands of the tsetse-fly However, there is strong circumstantial evidence that this is the route used by them Thus, although many thousands of infected flies have been dissected and examined by various workers, none has ever reported the finding of flagellates outside the alimentary tract (e g in the coelomic cavity) On the other hand, the migration of the flagellates from the mid-gut to the proboscis has been proved experimentally, while, on purely anatomical grounds, the only way the flagellates present in the proboscis can invade the salivary glands is via the hypopharynx That trypanosomes are actually capable of penetrating into the latter is evident from the fact that *Trypanosoma congolense*, which completes its development in the hypopharynx, can be demonstrated there in large numbers It would seem, therefore, that failure to detect trypanosomes of the *Brucei* group in the hypopharynx might be due to the fact that they use it only in transit to the salivary glands, and are not retained there

In discussing the origin of the inoculative method of transmission in pathogenic African trypanosomes, I suggested that it might have evolved from the contaminative method through a phase when the trypanosomes adapted themselves to mechanical transmission in a new vector However, recent studies on a non-pathogenic South American trypanosome of man and dog, *T rangeli*, indicate that in some cases this adaptation might take place in the same vector, since in this trypanosome the infective stages develop both in the hindgut and in the salivary glands of the Triatomid bug, which can transmit the infection both by fæcal contamination and through the bite

CYCLICAL TRANSMISSION OF HAEMOSPORIDIA

Ann Bishop Evidence has been brought forward by American workers that, in avian malaria, the ability of the gametocytes to infect mosquitoes

of the infection feed decreases the [illegible]

[illegible]

particles contained in the epidermis, but not those in other tissues Aphids can still become infective by feeding on irradiated leaves, but fasting does not increase the proportion that does and feeding periods of more than a minute are necessary. Although epidermal cells form a small part of the total leaf, extracts from irradiated leaves are much less infective than extracts from unirradiated [illegible]

[illegible]

the leaf epidermis, and the fact that fewer transmit after longer periods on the infected leaves is explicable because the aphids are then feeding from cells that contain less virus Aphids, particularly if they are feeding, soon cease to be infective with this type of virus and it seems that they can infect healthy plants only with virus particles retained in the tips of their stylets

This behaviour is not typical of all viruses Others are acquired only after insects have fed for 15 minutes or more on an infected plant. This is about the time the stylets take to penetrate to the phloem, and the likely explanation is that this group of viruses is most easily obtained from this tissue. Circumstantial evidence that these viruses are associated with the phloem comes from the fact that several of them produce lesions in this tissue but not in others. There is evidence, too, that some of these viruses need to be placed in the phloem by a vector before infection occurs, whereas those of the type described in the previous paragraph readily infect the epidermis If this is so, it could explain the fact that, although several viruses that cause phloem necrosis have been transmitted mechanically to their insect vectors by inoculating them with sap from diseased plants or from infective insects, they have not been transmitted mechanically to healthy plants

THE TRANSMISSION OF TRYPANOSOMES

R S Bray In the light of the recent discoveries in work on *T. rangeli* (= *T ariarii*) where the organism travels directly across the gut wall of *Rhodnius* to the haemocoelom and thus directly to the salivary glands, does Dr Hoare feel convinced that *Trypanosoma brucei* and its allied

mosquito either feeds with the fascicle in the lumen of the capillary, in which case the sporozoites from the infective insect would pass directly into the blood-stream, or else it feeds from a pool of blood coming from previously severed capillaries, in which case the sporozoites would be deposited in the blood pool and in the tissues Dr Willet and I have recently published a short note on the deposition of trypanosomes by the tsetse-fly, and we believe that we have shown that in such instances the trypanosomes are unlikely to be deposited directly in the blood-stream, but are probably delivered with the saliva into the blood pool and tissues

THE TRANSMISSION OF EXPERIMENTAL FILARIASIS

C. H Andrewes Could Dr Bertram say something more about the effects of continuous and intermittent exposure of cotton-rats to infection by microfilariæ?

D S Bertram The absence of microfilariæ in the blood of cotton-rats exposed to prolonged periods of re-infection has been shown to be related to inhibition of growth and the reproduction of microfilariæ by the adult female worms Their lengths may be as little as 3 cm, although they should have reached about 9 or 10 cm if the load of re-infections had not occurred Some females have been seen to be virtually sterile, [illegible] of worm growth and productivity is merely an overcrowding effect or due to host-reaction involving antibody Much is explicable merely as overcrowding effect

R M Gordon Dr Bertram has drawn attention to the fact that, in [illegible]

L. loa, in contrast to certain species of monkeys which appear to be

is adversely affected by the condition of the plasma at the peak of parasitaemia. The experiments were carried out by feeding *Aëdes aegypti* through [illegible] was not considered to be due to immunity, but rather that some factor or factors present in the blood and necessary for the further development of the gametocytes became exhausted as the infection developed.

R. S Bray. We too have felt that this effect was not due to immunity, but to some nutritional factor acting on the gametocyte. We had thought this factor might be a sheer lack of haemoglobin in the animals, which show a severe anæmia after the peak of parasitæmia. Obviously we must think again and in the terms of the plasma.

C. A Hoare. Professor Garnham has mentioned some of the barriers preventing malaria parasites from developing in unsuitable vectors As is known, the parasites of birds are normally transmitted by Culicine mosquitoes, whereas the human ones are transmitted by Anophelines. In an attempt to determine the factors responsible for this vector-restriction, a Russian worker (Levitanskaya, 1947) infected the human malaria vector, *Anopheles maculipennis*, with an avian parasite (*Plasmodium relictum*), and found that after 48 hours only the digested remains of ookinetes were present in the stomach, but none was anywhere near the peritrophic membrane. On the other hand, the normal avian malaria vector, *Culex*, infected at the same time, revealed ookinetes penetrating the peritrophic membrane and oocysts attached to the stomach This observer concluded that the insusceptibility of *Anopheles* to infection with avian parasites, and the refractoriness of *Culex* to human parasites, are not due to their inability to penetrate the peritrophic membrane, but are determined by factors present in the stomach of the mosquitoes, in the course of digestion of the blood

R. S Bray This is similar to Professor Garnham's experiences with *Hepatocystis kochi* and various possible vectors It is obvious that within any given system of a malaria parasite and an unnatural insect host sporogony may cease at any point from the first movements of the ookinete to the entry of the sporozoites into the salivary glands

R. M. Gordon Dr. Bray has referred to early observations made by Dr Lumsden and myself and later by Mr Griffiths and myself on the feeding mechanism of mosquitoes, and has asked whether I have anything further to add to these accounts. So far as the mosquito goes I have nothing to add to our original descriptions, which showed that the

larvæ develop in the mite, the mites require blood meals and the technical manipulations involved in this must add some casual causes of death and disability. A combination of all these points makes simple comparison of lightly and heavily infested batches of mites more difficult than might at first seem possible I think it is true to say that the mites tolerate well remarkably heavy infections of infective larvæ, but about the level of 90 or more worms per mite is certainly harmful, and in some mites even 40 or 60 larvæ seem to be enough to cause ill-effects in the vector But whether these instances of adverse effects are really due to the observed infection of large infective forms, or the attempted development of the unknown, and undeterminable, numbers of microfilariæ originally ingested (most of which fail to develop much, if at all), is difficult to determine.

GENERAL DISCUSSION

K Mellanby. Several speakers at this symposium have mentioned the dangers which improper use of statistical methods may produce These dangers are usually the fault of the biologist rather than the statistician, for unless adequate data can be given to a statistician, and unless he can be told what they are all about, he cannot be expected to give very much help Too many biologists expect to be able to hand over masses of undigested data for analysis and elucidation, and are then surprised if meaningless results are obtained

N Rees With regard to host resistance, is there any direct relationship between the number of invading organisms and the immunological response of the host? It is a fairly common practice in medicine to induce immunity by introduction of a small quantity of dead pathogenic organisms, or of organisms of a related but less virulent strain In these cases, is the conferred immunity effective against a mass attack of the live pathogenic strain?

F C. Bawden. Discussions on the effect of the size of the inoculum in determining whether or not infection occurs are, perhaps, simpler with plant than with animal pathogens, because infection of plants is not complicated by the concomitant production of antibodies against the pathogen Plants do have defence mechanisms, and different plants vary in their resistance to infection by a given pathogen, but they do not become resistant because they have been exposed to the pathogen The chances of getting infection established in a host are increased by increasing the quantity of a pathogen in the inoculum, and the problem is

zoologically good hosts for *L loa*. The second type of resistance is demonstrable in persons who, although they at first allow microfilariæ to appear in their peripheral circulation, later develop resistance or immunity.

K. Mellanby Are some rats more resistant than others to mites, and during the course of infection does the ability to tolerate mites change?

D S Bertram Cotton-rats differ in their usefulness as hosts of the mites. If, say, 200 or 300 female mites are released on a cotton-rat, the number recovered would usually amount to about 40 or 50 per cent, occasionally much lower, not infrequently as many as 80 per cent. There seems some tendency for an individual cotton-rat to be a good or a bad host—from the point of view of recoveries of the mites Some experimental work on exposing young cotton-rats to a series of experiences of being bitten by batches of mites over a period of a few months gave no clear indication of increasing sensitivity (as measured by recoveries of mites) after, I think, three or four months This work was then stopped, although, if it had been convenient to carry on longer, the results might have been more conclusive

[illegible]

D S. Bertram. Experience has lead me to conclude that this mite is not a very suitable creature for assessing the effects of its filarioid infection on its own vitality and survival Individual mites seem to tolerate very [illegible]

plants or man, because in the first case the disease may provide fundamental information about the biology of both host and parasite, whereas the second sort of disease, though it may be economically important, lacks the special interest and significance of the first sort

Ann Bishop In avian malaria it has been shown on several occasions that infections can be produced by the injection of single asexual parasites into the blood-stream of the host

R. F. Montgomerie. I am apalled by the picture which arises from the suggestion that infection is more likely to occur if ten pathologists have the opportunity to inject one rabbit compared with the effect of a single injection by one worker. Surely the effect on the animal is being forgotten Whether or not infection takes place with any particular dose must be related to other factors The condition of the animal and conditions in it are a material factor Black disease is caused by *Cl œdematiens* multiplying rapidly and producing its toxin at a site in the liver, but apparently not from recently acquired organisms Spores of *Cl œdematiens* are located in the liver of the sheep and only stimulated to cause disease by the damage caused by wandering larval liver flukes There is, then, no direct relationship between the acquiring of the infection and the occurrence of disease In swine erysipelas there is good evidence that the organism can frequently be recovered from the bone marrow of pigs which during life have shown no evidence of the disease Apparently some external factor creates the conditions under which clinical infection occurs. The injection of recently isolated strains of *E rhusiopathiæ* does not produce swine erysipelas in pigs In blackquarter in cattle the site of the lesion is not related to the route of entry

We must, therefore, not relate infection only to the dose of organisms

R. Cruikshank Does distemper virus spread by the aerial route?

R F Montgomerie There is evidence that the spread of distemper virus by the aerial route is not important In healthy ferrets, housed in bins 10 ft apart from those in which infected ferrets are kept, infection does not spread provided that the attendants carry out rigorous disinfection between their attending and handling the healthy and the infected animals

J L Harrison. In the discussion on Professor Lovell's paper and Mr Smith's remarks, the question arose as to what diseases in fact occurred among populations of wild animals I have been giving some attention to that question in a different guise—the cause of death of wild animals The question is an extraordinarily difficult one In the tropics, at least, one never seems to find either a sick or a dead animal from a normal population. In populations of the wild rat, *Rattus jalorensis*, I find that during mark-recapture experiments, in which animals are trapped and

to decide whether this happens because of some concerted action by the whole inoculum or by increasing the chances that one infective unit will survive the defences. Workers have often found that they could readily transmit a virus by its insect vector when test plants were colonised with many insects, but rarely when colonised with one; and they have suggested that infection can occur from the combined effect of several injections of virus, each of which alone would be less than a minimal infective dose. Whenever this suggestion has been examined critically, it has been proved false. Each infection is an independent event, and the probability that a group of insects will transmit is simply the probability that one or other of the members of the group would infect on its own. The idea of sub-minimal doses combining to give infections has been less canvassed with viruses, such as tobacco mosaic, that are mechanically transmitted and give countable local lesions, for dilution experiments with these, so far from suggesting any concerted action, show that the numbers of lesions obtained when inocula are diluted decrease by less than the factor of dilution. Whether the minimal infective dose is a single virus particle is uncertain, but there is circumstantial evidence that it is, and increasing [illegible]

enzymes or toxins, there is much more scope for a mass-action effect, and it is easy to see that many cells, although each one potentially as infective as the others, might act in concert to produce infection at one site, whereas acting singly all would be ineffective.

meiosis or mitosis, for they occur both in the pollen and the egg cells of infected plants There is, then, no need to postulate a late invasion of the developing seed by virus from the parent, it is already in the generative cells and virus-free plants can produce infected seed when their pistils receive pollen from infected ones

It is unusual, too, for plant viruses to pass from infective insect vectors to their offspring This is so even when the offspring are produced asexually, and there is no record of the viviparous young of aphids being born already infective A few leafhopper-transmitted viruses, however, regularly pass into eggs and can be inherited indefinitely in this way. These seem not to enter the sperm, and the young of virus-free females crossed with infective males were virus-free

R. M Gordon Mr Standen has asked me to emphasise the need for further research into the malacological aspects of schistosomiasis At the present time, it would appear that our knowledge concerning the snail vectors of schistosomiasis is similar to what was known of the vectors of malaria when, some 50 years ago, Ross discovered the transmission by mosquitoes

E. L Taylor I should like to raise a point of general interest in connexion with a part of Dr Standen's paper, and refer again to a point taken up by Mr Bawden after my paper presented yesterday To quote from Dr Standen's paper.

"The resistance to reinfection of the molluscan vector is not known Age resistance, in certain species at least, plays an important part Generally young snails are more susceptible to infection and resistance increases as the snails grow older, until infection becomes impossible This factor must play an important part in the maintenance of the vector strain, because infected snails are almost invariably sterile, and wholesale infection would lead to elimination of a snail community So, as long as the mature snails are immune to infection—whatever the cause may be—a plentiful supply of young is assured and both molluscan host and parasite may flourish "

This appears to me to be a clear example of the kind of adjustment to which I have referred It may be seen very clearly in the very great majority of successful and well-established parasites in the animal kingdom It is particularly apparent in nematodes, where immature hosts provide a susceptible part of the host community, ensuring the continuity of the parasite species, while the resistance developed by the adults ensures the continuity of the host species. In my opinion, it is very necessary when considering the building-up of host-parasite adaptations to think of species, and not to think of individuals It must be agreed that the resistance of these mature hosts is favouring the parasite species, as it ensures the continued presence of the host As it is a matter of mutual adaptation I think it is not stretching the use of words too far to say that it enables those two species to live happily together

kept for periods of one to three days, they suffer a death rate, in cages, of the same order as that which, according to my calculations, is suffered by the wild population The actual number of such deaths is small, but all appear to have been from pneumonia. The causes of these pneumonias have been investigated during the past year, and every one has been found to be of nematode origin We have been calling it " ascaris pneumonia ", more by analogy with the human condition than by actual knowledge of the nematode concerned

The identity of the death rates of the wild and the temporarily caged rats may be fortuitous, but this remains the only potentially fatal disease among these animals of which I have any knowledge.

P. K C Austwick It is clear that the attraction of ergot-infected flowers for insects is due to the formation of the sticky, sweet-smelling masses containing the *Sphacelia* stage of the fungus What is not at all clear is exactly why flies such as *Sciara thomæ* should visit uninfected flowers and so bring about the spread of the disease. Does anyone know what the habits of these Diptera are, and what causes them to alight on normal grass flowers? It is most noticeable that when epidemics of the disease caused by the entomophthorous fungus, *Empusa muscæ*, occur, great numbers of dead flies can often be found clinging to the flowering heads of grasses Is this because the dying flies have to settle somewhere and are more easily observed on grass flowers than on the ground, or is it because the flies normally frequent this habitat?

meiosis or mitosis, for they occur both in the pollen and the egg cells of infected plants. There is, then, no need to postulate a late invasion of the developing seed by virus from the parent, it is already in the generative cells and virus-free plants can produce infected seed when their pistils receive pollen from infected ones

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R. M. Gordon Dr Taylor has said that the host-parasite relationship implies that neither host nor parasite interfere with each other unduly. I agree that this is generally the case and that certain parasites can only escape from their hosts after the death of the latter: nevertheless, this does not necessarily imply any shortening of the host's life On the other hand, certain parasites, such as the larval tapeworm *Multiceps multiceps*, which can only escape from the host after death, unquestionably shorten the life of what appear to be their normal hosts

D S Bertram. In the text, on cotton-rat filariasis and its transmission, there are some points on this topic which I might briefly emphasise now. Those cotton-rats which have been exposed continuously for several months to re-infection show evidence of repeated re-infection, and yet have very low or negative microfilarial counts in their blood-stream, become thin, lethargic creatures about half the normal weight of uninfected rats of similar age and sex The adult worms in such rats are inhibited severely in growth and productivity. In such epidemiological conditions the mammal and the helminth parasite seem to be suffering adversity, but the vector, the mites, can feed freely on the rats with no risk of lethal results from the very heavy infections with the filarial larvæ. The advantage is to the mite. But cotton-rats exposed to infrequent intermittent transmission remain alert and active and of normal weight although harbouring large numbers of quite well-grown, very productive adult worms which maintain extremely heavy microfilarial infections in the blood-stream of the cotton-rats. Neither the mammal nor the helminth appears to be inconvenienced, but in these conditions the vector-mite is, at least, at greater risk of acquiring very heavy and lethal

pathologists, who can provide him with examples of viruses that have both [illegible]

there are any such plant viruses they probably account for only a small fraction of the total, for there seems little point in considering this possibility unless a virus multiplies in its vector, and few plant viruses do. These few seem to maintain themselves as readily in insects as in plants, and some more so because they are transmitted through the eggs of insects, but not through the seeds of plants, also they have been transmitted experimentally by inoculation to insects, but not to plants Except by inheritance, there is no evidence of spread from insect to insect, but this may have happened in the past and the method may have been lost and replaced by the ability of insects to acquire the virus by feeding on infected plants This all fits nicely with the idea that they are better " adapted " to insects than plants, but equally there may have been other methods of spread between plants that have been replaced by the current vectors As always, there is too little evidence to interpret the present position in evolutionary changes unless some unwarranted, subjective concept is introduced

The second possibility I had in mind has, I think, greater potentialities It was not that plant viruses originated in insects, but simply that the insects were responsible for originating plant virus diseases The plant viruses whose constitutions are known are nucleoproteins and their nearest analogues seem to be " normal " nucleoproteins The migratory and feeding habits of insects admirably fit them for transferring components from cells of one individual or species to another, although these components may not have been pathogenic, or even parasitic, in the cells where they originated, their introduction by insects into new cells may often have started the sequence of events that has culminated in the conditions we currently recognise as transmissible virus diseases

P Tate. In addition to the viruses which insects transmit to other organisms, in which they are pathogenic although they are not pathogenic to the vector insects, there are purely insect viruses which are highly pathogenic to the insect host. How does Dr Andrewes think such viruses are related to those he suggested evolved from non-pathogenic insect forms which became pathogenic when in the course of evolution they became adapted to non-insect hosts?

J L. Harrison First I would like to thank Dr. Andrewes for introducing those very useful terms, " vertical ", " horizontal ", and " zig-zag " transmission We in the Scrub Typhus Research Unit in Malaya have long been dissatisfied with the popular term " transovarial " as applied to mite-typhus, and have felt the need of a non-committal expression.

I understand Dr. Andrewes to suggest that the rickettsiæ primitively showed a zig-zag transmission which may have evolved to horizontal and vertical methods. A few years ago I would have disagreed with that view, and to explain why my views have changed I should like to explain some of the work and ideas of my colleague Dr. J. R. Audy in Malaya

The rickettsia of mite-typhus or scrub-typhus is transmitted by the bite of a trombiculid mite whose normal host is a rat. We know of "jungle" infections in forest rats and their mites. When the forest is cleared, the organism is taken up by a grassland rat and mite, and the accidental intrusion of man into this cycle gives scrub-typhus. Our tentative view is that this infection has been taken up by town rats and their fleas (fleas are rare on Malayan field rats) and evolved into the flea-typhus or [illegible] This [illegible] would suggest evolution from vertical to zig-zag transmission. The progeny of one infected female mite have, however, been bred in the laboratory, and it is found that although the infection is transmitted vertically for at least six or seven generations (that is as far as the experiment has been taken), the transmission is not to all of the progeny Inbred strains of some groups of eggs show no further infection. I cannot give a good estimate of the proportion of progeny infected, the figures have not yet been worked out, but I should say that it is certainly less than 10 per cent I would emphasise that I am reporting the incomplete work and ideas of my colleagues, not my own work

My point is that although vertical transmission occurs in this the most primitive member of the typhus fevers, it appears to be inefficient, and zig-zag transmission would be necessary to maintain the infection The example, therefore, supports Dr Andrewes' views.

B W Lacey Although congenital transmission of rickettsiæ in the mite may be questioned, its occurrence in the tick seems certain. Rickettsiæ of tick typhus (Gear and de Meillon, 1941) and Q fever (Davis, 1943) and spirochætes of relapsing fever (Mollers, 1907) have all been followed through three generations of ticks

Davis, G. E 1943 *Publ Hlth Rep, Wash*, 58, 984
Gear, J and de Meillon, B 1951. *S Afr med J*, 15, 389
Möllers, B 1907 *Z Hyg InfecktKr*, 58, 277.

ulum by making the microfilariæ less accessible to the flies A similar ct in cotton-rat filariasis follows prolonged exposure to re-infection, h its associated very low densities of microfilariæ in the blood-stream, indeed their absence altogether Transmission of both infections is ly to be minimised, if not stopped, by these effects of re-infection on microfilarial population, but the mechanism is different for each species filarioid worm In one case, it is microfilarial migration, and, in the er case, microfilarial elimation which threatens the continuity of nsmission

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